VOL. CLX, No. 3 SEPTEMBER, 1920 No. 582

1820 CENTENNIAL YEAR 1920

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THE

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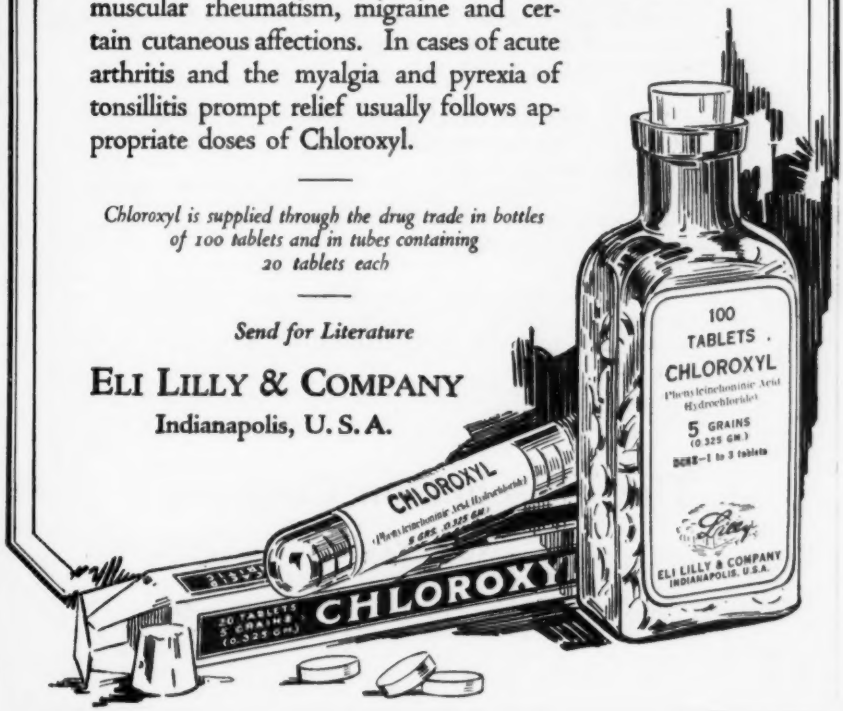

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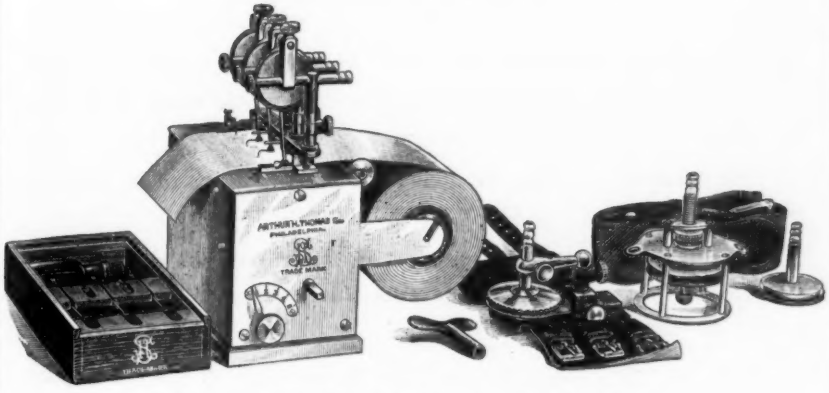

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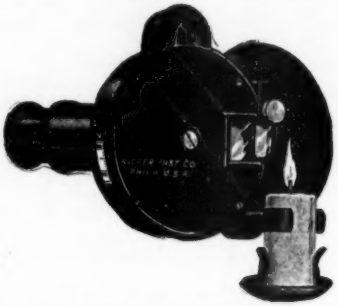

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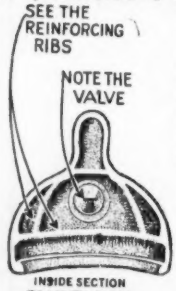

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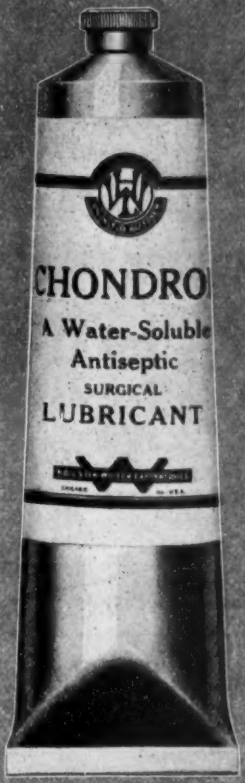

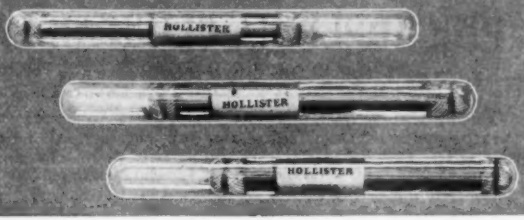

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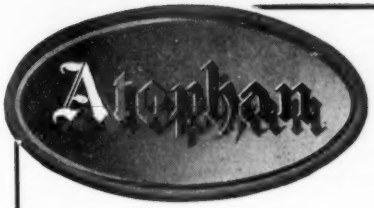

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

SEPTEMBER, 1920

ORIGINAL ARTICLES.

THE BLOOD-SUGAR TOLERANCE TEST AS AN AID IN THE DIAGNOSIS OF GASTRO-INTESTINAL CANCER.[1]

By Julius Friedenwald, M.D.,

and

George H. Grove, M.D.,

Baltimore, Md.

The great difficulty arising in the diagnosis of gastro-intestinal carcinoma, especially in the early stages, has long been recognized. In spite of our modern methods of investigation, including the most recent tests, the diagnosis in many instances remains obscure often until late in the progress of the disease and is frequently not revealed until exploratory incision establishes the true nature of the affection. Any additional help therefore which may lead to the solution of this difficult problem cannot but be of the greatest value. In the blood-sugar tolerance test we believe there has been added a further step in advance in this direction.

The fact that a high blood-sugar content is usually observed in patients affected with carcinoma has been known for many years. Freund,[2] in 1885, was the first to point out on the basis of seventy blood-sugar investigations that there is always a hyperglycemia in this disease; on the other hand he was unable to observe a similar condition in sarcomatous patients; he therefore recommends on this

[1] Read at the Meeting of the Association of American Physicians, Atlantic City May 4, 1920.

[2] Allgemeine Wiener med. Zeitung, 1885, No. 9, S. 102.

account that blood-sugar estimations be made as an aid in the differential diagnosis between the two affections.

Trinkler[3] investigated the blood-sugar content not only in carcinomatous patients but also in patients affected with other diseases, such as typhoid, pneumonia and tuberculosis. In these observations there were 109 analyses, which were divided into two groups: (1) the estimation of sugar in the blood collected at operation, and (2) in that obtained at autopsy. A far greater hyperglycemia was observed in carcinoma than in other diseases.

The following table of Trinkler is interesting, as it presents the average, maximum and minimum percentage of sugar in the blood as observed by him in various diseases:

	Average.	Maximum.	Minimum.
Cancer	0.1819	0.3030	0.1023
Typhoid	.0950	.1022	.0875
Lobar pneumonia	.0943	.1092	.0813
Dysentery	.0838	.0915	.0796
Heart disease	.0737	.0897	.0664
Peritonitis	.0701	.0917	.0450
Tuberculosis	.0652	.0817	.0450
Syphilis	.0553	.0748	.0449
Nephritis	.0489	.0559	.0311
Uremia	.0375	.0559	.0311

Trinkler arrived at the following conclusions:

1. Hyperglycemia is always present in cancerous patients.

2. In carcinoma of the internal organs there is always a far greater hyperglycemia than in carcinoma of the skin or mucous membrane.

3. The cachexia of carcinomatous patients bears no relation whatever to the increase in blood-sugar.

In recent years many important investigations have been published by various observers regarding the significance of alimentary hyperglycemia as a test of sugar tolerance in health as well as in disease.

Jacobson[4] was the first to point out the importance of such investigations. He presents his results in 14 normal individuals following the administration of 100 gm. of glucose, and observes that an increase in blood-sugar occurs within 5 minutes after the administration of the glucose rising to its height in 30 minutes, which is followed by a gradual decline to the normal level in approximately 120 minutes, the blood-sugar increasing thus from 0.10 per cent. to 0.22 per cent. in 30 minutes and then gradually falling again to 0.12 per cent.

Hopkins,[5] working along similar lines, observed in his investigations that in health a moderate rise in blood-sugar (0.11 to 0.156 per cent.) occurs after the ingestion of 100 gm. of glucose reaching

[3] Centralblatt f. die medicinishen Wissenschaften, 1890, No. 28, S. 498.
[4] Biochem. Ztschr., 1913, S. 411.
[5] Am. Jour. Med. Sc., 1915, cxlix, 254.

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its height in from 30 to 120 minutes, and again quickly subsiding. He also notes that hyperglycemia is most pronounced in certain diseases, as in diabetes, pancreatic, nephritic and pituitary cases, in pneumonia, apoplexy, typhoid, tuberculosis and cancer.

A very elaborate and careful study of alimentary hyperglycemia has been published by Hamman and Hirschman.[6] These observers have pointed out that in normal individuals after the ingestion of 100 gm. of glucose the blood-sugar rises to a maximum concentration not exceeding 0.150 per cent., reaching its height in 30 minutes, which is followed by a gradual fall.

Similar observations were carried on in various diseases, *i. e.*, diabetes, nephritis, disturbances of the thyroid gland and hypophyseal functions, with rather definite results, and in some of these conditions rather typical curves were constructed, which are of considerable diagnostic significance.

The first careful investigations as to the glucose tolerance in cancer were published by Rohdenburg, Bernhard and Krehbiel.[7] Sugar determinations were made of the blood just before and again in 45 minutes, and 120 minutes after the ingestion of 100 gm. of glucose. While the normal individual presents an increase in the blood-sugar percentage, reaching its maximum in 45 minutes, which then gradually recedes to the normal, the cancerous patient begins with a normal blood-sugar, rising steadily in 45 minutes after the ingestion of the glucose to 0.18, or 0.2 per cent., and continues to rise or remain stationary for 120 minutes after the ingestion of the glucose, the percentage being either as high as the 45-minute reading or higher, reaching 0.28 per cent. or even to 0.35 per cent. The blood-sugar content then gradually begins to recede, approximating normal in from 180 to 240 minutes. This character of curve was observed in 24 cases of carcinoma and in 1 case of sarcoma, and was not found in other diseases.

According to these observers the sugar tolerance bears no relation to the location of the tumor, for primary carcinoma of the lung, sigmoid, stomach, heart and other organs all present similar findings.

Benedict and Lewis[8] report their observations in the blood-sugar content in 53 patients affected with malignant growths; the blood being taken 180 minutes after the ingestion of food. Of these cases 10, or 36 per cent., revealed a marked increase in blood-sugar, ranging from 0.12 to 0.16 per cent. At least 49 per cent. of the cases showed a tendency to hyperglycemia. According to these investigators there was noted a steady increase in the blood-sugar content as the disease progresses, reaching a maximum just prior to death, the hyperglycemia being in all probability a result of a constant demand of the growing tumor for carbohydrates.

[6] Arch. Int. Med., November, 1917, vol. xx.
[7] Jour. Am. Med. Assn., May 23, 1919, 1528.
[8] New York Med. Record, October 19, 1914, lxxxvi, 650.

Williams and Humphreys[9] observed a moderate increase in blood-sugar in 9 cases of carcinoma after the ingestion of an ordinary meal; they give no determinations following a dextrose meal; these investigations are therefore of but little clinical value. Cammidge[10] also calls attention to the hyperglycemia present in carcinoma, believing that in explanation of this finding there may be at hand a faulty functioning of the endocrine glands for a "similar hyperglycemic response followed by a delayed fall to normal has been observed in hyperthyroidism and exophthalmic goiter." Very recently, and since the completion of our study, Rohdenburg, Bernhard and Krehbiel[11] have published the results of an elaborate investigation on sugar mobilization based upon 228 cases. These authors call attention to three different types of reaction accompanying the sugar-tolerance test: In the first type, termed 1, the blood-sugar at the 45-minute interval rises above the zero hour figure and at the 120-minute interval is as high or higher than the 45-minute interval. In type 2 the rise in the 45-minute interval occurs as in type 1, but at the 120-minute interval the curve falls almost or completely to the original figure. In type 3 the initial sugar concentration is higher than or the same as that at 45 minutes, and the 120-minute interval shows a return to the original figure more or less complete, sometimes going even higher.

In nephritis 75 per cent. of the cases gave type 2 reaction; 60 per cent. of the tuberculous cases gave type 1 reaction; 72 per cent. of the cases of syphilis showed type 2; 60 per cent. of the diabetic type 2 curve; 66 per cent. of the pregnancy cases gave type 1 reaction. These investigators have materially modified their previous views regarding the blood-sugar concentration in cancer. They found that 61 per cent. of gastric carcinomata and 50 per cent. of intestinal carcinomata gave type 1 reaction, and are of the opinion that the high sugar concentration observed in gastric carcinomata is in no way due to cachexia. They do not consider that any of the three types should be considered as diagnostic of any pathological condition, though generally conditions associated with increased cell growth present a greater percentage of type 1 reaction.

The great difficulties arising in the diagnosis of gastro-intestinal carcinomata, especially in the early stages, have led us to make a further study of the blood-sugar tolerance test as an aid in the differential diagnosis between carcinoma and other diseases of the abdominal organs, realizing full well, from the work of Rohdenburg and his co-workers, that a test of this character can serve only as an additional help in diagnosis, but must in no way be considered as specific of any disease.

In order to establish the practical utility of the blood-sugar

[9] Arch. Int. Med., 1919, xxiii, 537.
[10] Practitioner, February, 1920.
[11] Am. Jour. Med. Sc., April, 1920.

tolerance test the method employed must be, though necessarily accurate, so simplified as to be easily carried out and not too time-consuming. In our examination we have followed the plan recommended by Hamman and Hirschman, as well as that of Rohdenburg, of giving after a night's fast 100 gm. of dextrose thoroughly dissolved in 300 c.c. of black coffee without additional sugar. The blood was withdrawn for examination by puncture from the arm vein just before and again in 45 minutes, and 120 minutes after the administration of the dextrose. The blood-sugar was determined by the Epstein method by employing a standardized apparatus which had been thoroughly tested as to its accuracy; we feel that by this method a simple as well as an accurate means is afforded for estimating blood-sugar. The advantages of this method are well known. It requires but 10 to 15 minutes to complete a determination of sugar, necessitating but a very small quantity of blood, and does not entail the employment of an expensive colorimeter, which thus renders the method especially useful for clinical work. Again, the slight error common to our estimations can be of but minor significance, inasmuch as the test is a comparative one of at least three estimations conducted in each individual case, and in addition all of the determinations were made by the same individual under similar conditions. The urine was examined at varying periods in many instances, but sugar was but once observed in any of our cases up to 120 minutes after the ingestion of the glucose; occasionally it was present after 180 minutes.

In our investigations the blood-sugar tolerance was studied in 32 cases of carcinoma of the gastro-intestinal tract. All of the cases were typical of this disease; of these 17 were operated on and the diagnosis was thus confirmed, and in the remaining cases there were definite palpable abdominal masses in addition to the usual physical signs present in this affection; and the examination of the gastric contents as well as the roentgen ray and final outcome presented confirmatory evidence in every instance. Of these cases there were 19 of gastric carcinoma, of which there were 11 with obstruction at the pylorus, 1 at the cardia and 7 presented no obstructions; there were 9 cases of carcinoma of the stomach, with metastases in the liver and other abdominal organs; 2 of carcinoma of the rectum and of the cecum and 1 of the face and tongue. In addition, blood-sugar tolerance tests were made in 3 cases of uterine carcinoma; 1 case of breast cancer; 1 case of carcinoma of the prostate and spine; 1 case of uterine fibroid; 2 cases of sarcoma (1 of the jaw and 1 of the leg); in 8 cases of peptic ulcer; 2 cases of syphilis of the stomach; 3 cases of diarrhea and dysentery; 8 cases of achylia gastrica and chronic gastritis; 4 cases of cholelithiasis; 2 cases of chronic appendicitis; 11 cases of enteroptosis; 5 cases of nervous dyspepsia and 5 cases of intestinal stasis and mucous colitis, making 88 cases in addition to the 4 perfectly normal individuals studied for purposes

of comparison. The sugar tolerance curves as observed in our cases may be classified into the following groups:

1. **The Normal Curve.**—In normal individuals after the ingestion of 100 gm. of dextrose the blood-sugar content rises from 0.09 or

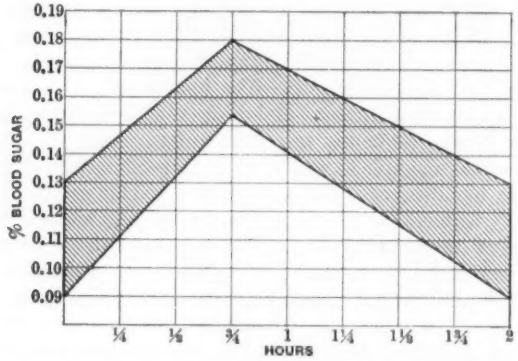

CHART I.—Maximum, minimum and average normal blood-sugar tolerance curve.

even less to a height not usually above 0.165 per cent. within 45 minutes, falling usually more gradually within 120 minutes to about the level as that observed in the fasting state. This character of

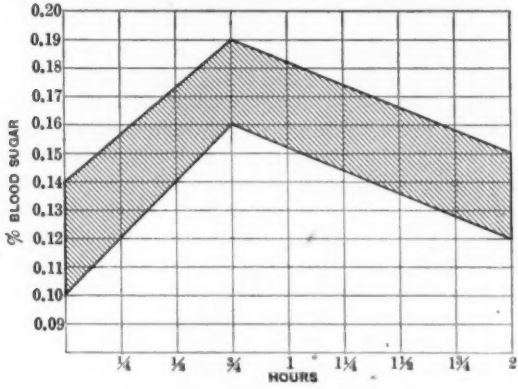

CHART II.—Maximum, minimum and average atypical normal curve.

curve was observed not only in normal individuals but also in the non-cancerous digestive disturbances other than those which have been classified in the following group. The two sarcoma cases also presented normal curves:

2. **The Atypical Normal Curve.** In certain individuals, often those affected with an achylia gastrica, an atypical normal curve is observed in which the blood-sugar content presents practically normal values in the fasting state, ascending to a height of from 0.16

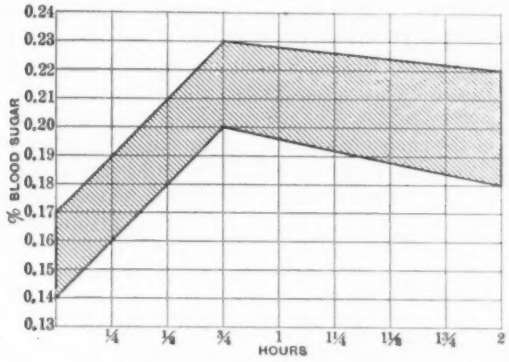

CHART III.—Maximum, minimum and average intermediate blood-sugar curve.

to 0.18 per cent. within 45 minutes after the ingestion of the dextrose, falling slowly within 120 minutes to a level of from 0.13 to 0.15 per cent., but not any lower. This form of curve was found not

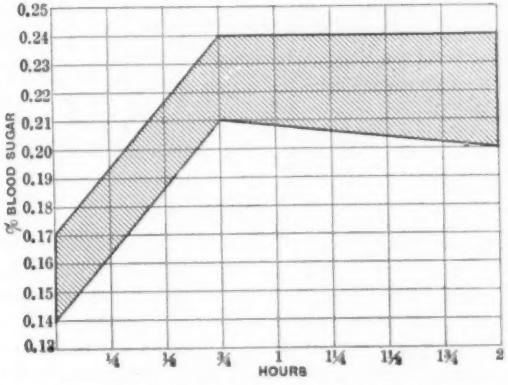

CHART IV.—Maximum, minimum and average blood-sugar tolerance curve in carcinoma of the gastro-intestinal tract.

only in our achylia cases but also in the cases of pyloric stenosis of benign origin.

3. **The Intermediate Curve.** The intermediate curve is usually observed in cases of carcinoma not associated with the gastro-

intestinal tract, in which the blood-sugar content presents comparatively high values even in the fasting state of 0.14 to 0.17 per cent., and in which after the ingestion of 100 gm. of dextrose there is an initial rise to a height of from 0.2 to 0.23 per cent. within 45 minutes, followed within 120 minutes by a fall to a level of from 0.18 to 0.21 per cent., never descending at this time to the level observed in the fasting state. The intermediate curve was observed by us in 3 cases of uterine carcinoma, 1 case of carcinoma of the prostate and spine and 1 case of carcinoma of the breast.

4. **The Cancer Curve.** The cancer curve is usually observed in carcinoma of the gastro-intestinal tract in which even in the fasting state there is a high sugar content of from 0.14 to 0.17 per cent., followed after the ingestion of the 100 gm. of dextrose by an initial rise of from 0.21 to 0.24 per cent. or higher within 45 minutes,

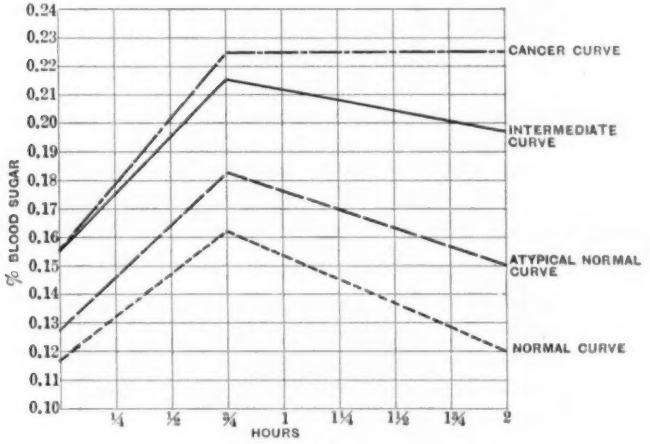

CHART V

remaining at this level for at least 120 minutes, and at no time during this period falling below 0.20 per cent. This form of curve was observed in all of the cases of cancer of the gastro-intestinal tract, but was not present in any one of the other 55 examinations, including 5 cases of carcinoma outside of this tract nor in 2 cases of sarcoma nor in any of the 45 cases of benign affections of the gastro-intestinal tract. The form of curve present therefore in gastro-intestinal cancer is rather characteristic and can usually be distinguished from that observed in cancer of any other region of the body or from that of non-malignant disease. It should be noted, however, that in cases of suspected carcinoma of the gastro-intestinal tract in which the curve is not absolutely characteristic or is of the intermediate type that a second examination made after a short interval of time will usually reveal the true condition.

We have not had an opportunity to observe early cases of cancer of the gastro-intestinal tract according to this test except in a single instance, but we are under the impression that the test is quite as definite in early as in late cases, as it is usually positive whether cachexia exists or not or whether there is but a slight or a marked involvement of the organs. It is important to note that diabetes, nephritis, tuberculosis and disturbances of the thyroid should always be excluded before the tolerance test is undertaken, inasmuch as hyperglycemia is frequently present in these affections. Inasmuch, however, as this test is to be utilized only as a means of differentiation between carcinoma and other diseases of the gastro-intestinal tract, many conditions associated with hyperglycemia need not be taken here into consideration.

TABLE PRESENTING THE PERCENTAGES OF BLOOD-SUGAR OBTAINED IN THE 32 CASES OF CANCER OF THE GASTRO-INTESTINAL TRACT.

No.	Name.	Cancer of	0 Hour.	45 Min.	120 Min.
1	M. J. B.	Pylorus	0.141	0.250	0.238
2	G. F. B.	Liver and stomach	.12	.198	.192
3	S. S. B.	Stomach	.163	.268	.278
4	T. C.	Liver and stomach	.147	.191	.194
5	G. C.	Liver and stomach	.162	.204	.201
6	M. H. C.	Liver	.196	.240	.243
7	D. E. D.	Stomach	.178	.364	.332
8	C. E. D.	Pylorus and lesser curvature	.131	.187	.183
9	J. A. D.	General carcinomatosis	.161	.258	.255
10	E. G.	Uterus and rectum	.125	.187	.194
11	D. G.	General carcinomatosis	.161	.250	.256
12	H. G.	Liver and stomach	.163	.214	.208
13	W. K.	Pylorus	.149	.198	.194
14	C. S. I.	Cecum	.155	.226	.258
15	P. J.	Pylorus	.142	.187	.179
16	F. L.	Rectum	.202	.300	.264
17	J. L.	Pylorus	.176	.252	.266
18	C. J. M.	Stomach	.158	.210	.210
19	H. C. P.	Stomach	.142	.262	.247
20	G. C. P.	Stomach	.164	.242	.238
21	M. M.	Pylorus	.138	.204	.204
22	R. E. M.	Stomach	.142	.194	.192
23	E. R.	Pylorus	.141	.192	.174
24	I. P. S.	Liver and stomach	.121	.162	.153
25	S. F. L.	Tongue	.384	.497	.497
26	M. S.	Cardia	.131	.180	.224
27	C. S.	Stomach	.206	.266	.256
28	J. T. T.	Pylorus	.171	.239	.240
29	S. V.	Liver and stomach	.139	.214	.206
30	S. W.	Pylorus	.162	.198	.194
31	E. W.	Stomach	.154	.192	.178
32	W. A. Z.	Stomach	.161	.220	.218

The value of the test is well illustrated in three of the cases of this series; we append a brief abstract of the histories of these cases:

CASE I.—M. R. (No. 4857), male, aged fifty-four years, had been complaining of stomach trouble for some months; he was affected with nausea and vomiting; much discomfort after meals

with eructations, flatulency, loss of appetite and loss of flesh (twenty pounds). Recently he had frequently vomited food taken the day previously. On physical examination the liver was found enlarged and there was a definite resistance in the upper right quadrant. The examination of the gastric contents revealed but small amounts of free hydrochloric acid, and there was marked retention. On roentgen-ray examination there was found an enormously dilated stomach, with a large filling defect and a 1080-minute retention. The diagnosis of pyloric obstruction, due to ulceration and possibly to a malignant growth, was made. The sugar tolerance test revealed a normal curve pointing definitely against carcinoma. At operation, performed February 21, 1920, by Dr. J. M. T. Finney, a non-malignant pyloric stricture was found.

CASE II.—E. S. (No. 5002), male, aged forty-eight years, had been affected with indigestion for the past six months. He had lost ten pounds in weight, had nausea, vomiting, loss of appetite and complained of weakness and of the passage of blood in the stools. On physical examination of the abdomen nothing abnormal was determined. His gastric secretion presented a true achylia. The stools contained occult blood and the roentgen-ray revealed a large filling defect at the pylorus, involving a large area on the lesser curvature. The diagnosis of carcinoma was made. The sugar tolerance test, however, presented a perfectly normal curve. At operation, March 1, 1920, by Dr. J. M. T. Finney, a chronic gastritis with pylorospasm was revealed.

CASE III.—M. M. C. (No. 4652), male, aged sixty-one years, complained of indigestion for at least four years, which had recently become more aggravated; there was present loss of appetite, eructations of gas, pressure and fulness after meals, and loss of flesh (twenty pounds). On physical examination of the abdomen the liver was found enlarged; there were no palpable masses present. The gastric secretion presented a low total acidity 10 to 12, with an absence of free HCl. The roentgen-ray examination revealed a large filling defect at the pylorus and on the lesser curvature, on account of which a positive diagnosis of carcinoma was made. The sugar-tolerance test, however, presented an atypical normal curve. The Wassermann test was positive and the patient has recovered after having undergone an antiluetic treatment.

In considering the possible causes that may be responsible for the delayed tolerance curve in the blood in cancer, two possibilities have been suggested by Dr. Charles E. Simon:

1. Whenever increased cell production is maintained there must necessarily be some source of energy available, and inasmuch as the most potent source is dextrose, it is quite conceivable that a special call might be made on the part of the multiplying cells upon the liver for an increased supply of dextrose. Should the liver respond to this call, but owing to the defective blood supply in a carcinoma only a small portion of the available sugar should

be utilized, a hyperglycemia might develop. This hyperglycemia does not occur in sarcoma, which may be explained on the basis that in this disease there is a more or less abundant blood supply, whereas in carcinoma the reverse is observed. The available dextrose in sarcoma would on this account be utilized and a hyperglycemia would consequently not develop.

2. As a second possibility one could conceive that a hormone might be liberated into the circulation by the carcinoma, in consequence of which the normal power of oxidation of the sugar on the part of the tissues at large or of certain special ones, like the muscle tissues, might be impaired; in consequence a hyperglycemia could not only result under normal conditions of carbohydrate supply but also when an increased quantity of dextrose is made available; in addition it might be possible that such a factor might be responsible for the defective nutrition of the body at large and thus for the progressive loss of weight associated with cancer.

From our study of the blood-sugar tolerance test in health, as well as in the various affections of the gastro-intestinal tract, we believe that the following conclusions may safely be drawn:

I. There is present in carcinoma of the gastro-intestinal tract usually a rather characteristic curve of sugar tolerance which differs somewhat from that observed in carcinoma of other regions of the body. The curve of this affection usually presents a high sugar content even in the fasting state, followed by an initial rise up to 0.24 per cent. or higher within 45 minutes after the ingestion of the dextrose remaining at this level for at least 120 minutes, and at no time during this period falling below 0.20 per cent.

II. The sugar tolerance test is rather distinctive, so that it may render valuable assistance in a large proportion of cases as a means of differential diagnosis between carcinoma and other diseases of the gastro-intestinal tract.

III. The opportunity has not been afforded to test a sufficient number of early cases of cancer of the stomach and intestines according to this method, so that as yet the value of this test as a means of early diagnosis has not been established; nevertheless, as positive curves occur equally whether cachexia exists or not, or whether the extent of the involvement be slight or great, we are under the impression that the results may be quite definite even in the early cases of the disease. This question, however, requires further study.

IV. Finally, while we fully realize that this test is not specific of carcinoma and cannot be relied upon alone without entering into the clinical aspects of the disease, and that there are cases of carcinoma in which negative findings occur or non-malignant conditions in which the results are positive, nevertheless we are of the opinion that when properly performed the blood-sugar tolerance test may be of considerable diagnostic help in obscure cases of carcinoma of the gastro-intestinal tract.

CERTAIN POINTS IN THE DIAGNOSIS AND TREATMENT OF PULMONARY TUBERCULOSIS.[1]

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At the very beginning of my talk I wish to express my gratitude for the opportunity I have been given to address tonight so many practitioners of medicine. It has become a favorite pastime of a few tuberculosis specialists to berate, to bait, so to speak, the general practitioner, for his ignorance of tuberculosis. If this poor individual has had, for example, under his care two patients in whom not only physical signs but symptoms as well were equivocal, about whom no man without generous funds or a hospital staff at his command could speak authoritatively, and if by chance this maligned worker sends them to different specialists, he may be blamed by one for even suggesting tuberculosis, for branding the patient, as some put it, with the stigma of tuberculosis when he has not got it, and censured by the other for his ignorance in not recognizing a clear case of tuberculosis. It is sad, but true, that the reputation of many of us depends upon the cook and the indigestion that follow the meal.

Those of you who have read that delightful book, *The Future of Medicine*, by Sir James Mackenzie, who writes at an age when most men dwell in retrospection, will recall what he says of the general practitioner, of his importance in and value to the advancement of medicine. He alone sees disease at its very inception. He discovers the spring, and, as I have said, is often criticized for not doing the impossible, for not determining forthwith into which river it will eventually flow. You have, as Sir James points out, exceptional opportunity of studying disease long before it reaches the consultant, months before the classical picture enables the attending physician in the large hospital to make, without undue mental effort, a diagnosis. Our need today calls less for workers in the laboratory, less for well-trained attending physicians, than it does for trained practitioners who are willing to study carefully, and in detail, symptoms which may indicate eventual disease or may peter out in a state of good health.

The physical signs of all pulmonary disease were worked out by the study of pulmonary tuberculosis. P. C. A. Louis, of Paris, who revolutionized not only our knowledge of tuberculosis but also the method of attacking clinical disease, based his work on a study of only one hundred cases of pulmonary tuberculosis.

It seems then that time spent on so common, on such an uninter-

[1] Read at a meeting of the New York Physicians' Association, New York, March 25, 1920.

esting disease as pulmonary tuberculosis, has borne fruit in the past, and time applied to it today by the general practitioner may even yet reward him as richly in the future as it has done others in the past. I say this knowing full well the enormous energy a general practice consumes, and realizing fully that but a small fraction of us have energy enough for practice and little if any left for such study. I simply wish to place before you the opportunity every practitioner has open to him and not to criticize any of you for failure for one or several reasons in not accepting it.

I shall not attempt tonight to present to you any comprehensive discussion of diagnosis or the treatment of pulmonary tuberculosis, but shall single out here and there certain phases that have interested me.

Diagnosis.—The diagnosis of pulmonary tuberculosis, curiously enough, grows more instead of less difficult as time goes on. I can recall the day when a patient with cough and expectoration, and a few fine rales, possibly above the clavicle, was always considered to be suffering from pulmonary tuberculosis. A little later it was pointed out that influenza might produce such a condition, and then for a time we gave all patients admitted to Trudeau, who had never had tubercle bacilli found in their sputum, the subcutaneous tuberculin test. Shortly after this the cutaneous and ophthalmic tuberculin tests were introduced, and if they were of no other help they certainly stimulated the study of the tuberculin reaction. This study and the fact that, given, so to speak, in the dark, tuberculin occasionally set up reactions, which, while never permanently dangerous, were very diagreeable and uncomfortable, led us to use the test less and less. About this time roentgen-ray study of the lungs was introduced, and, as many of you recall, it brought about, first, wonder, then opposition (the opposition of ignorance, if I may so term it), and finally acceptance. Complement-fixation to various specific tuberculous antigens was next added to our armamentarium and helped exclude certain confusing cases. Few of you have not worked at one time or another on some draft board, and most of us appreciate the advance in our knowledge of pulmonary tuberculosis that the study of such large numbers of men has brought about. It has emphasized particularly that chronic tuberculosis may be active and of moment, or inactive and capable of great physical strain without relapse.

For some years we have had sent to us at Trudeau a group of cases that formerly we should have labelled at once "incipient" and dismissed all further thoughts of their diagnosis from our minds. Today more careful study shows that many of these patients have no discoverable pulmonary tuberculosis. Formerly some doubtful cases passed through the institution for the reason that the diagnosis never was but always to be made. To obviate this error we introduced a diagnostic clinic, held weekly, attended by all the staff at

which all data about each patient is presented. This includes a full history, data obtained on complete physical and roentgenologic examinations, sputum examinations (concentrated if necessary), complement-fixation tests for tuberculosis and syphilis, adrenalin test of Goetsch, and tuberculin tests, intradermic and subcutaneous, if deemed necessary. These data, collected largely by different workers, who are usually unaware of the others' findings, are placed upon a blackboard, and are used to determine (1) if tuberculosis infection is present (positive intradermic tuberculin test), (2) if clinical tuberculosis exists, and (3) if the disease is active or inactive, or potentially active, during the first week of residence in the institution.

It seems needless to state that in some cases we can neither affirm nor deny the presence of pulmonary tuberculosis, though rarely do we have a patient who fails to react to the intradermic tuberculin test. I might say in passing that a diagnosis of tuberculosis infection is considered of no moment clinically. We have had to employ and to define various terms. "Non-tuberculous" we have used as implying:

1. No occurrence of tubercle bacilli in the sputum.
2. No persistent moderately coarse rales in the upper chest.
3. No parenchymatous roentgen-ray changes.
4. No history of hemoptysis.
5. No history of pleurisy with effusion.
6. Failure to react to a second subcutaneous dose of 10 mg. of old tuberculin.

If the patient reacts to a subcutaneous dose of tuberculin and has none of the other data, we diagnose him as having "suspected tuberculosis." If some of the data are not obtainable and the remainder negative we call the case "tuberculosis unwarranted."

There is still but one pathognomonic sign of pulmonary tuberculosis, the occurrence of tubercle bacilli in the sputum. Errors, that others as well as ourselves have committed, have led us to believe that one or two or even three tubercle bacilli in a specimen must be confirmed by two observers. We also hold that it is far safer to verify at once by a second examination the presence of tubercle bacilli in the sputum. With the ample facilities afforded today by the private and public health laboratories it is inexcusable for any of us to omit this method of diagnosis. I have been positive from a study of the symptoms and of the physical signs that a patient did not have pulmonary tuberculosis. The roentgen-rays were similarly against it, but tubercle bacilli were found in the sputum on repeated examinations. It will never harm any patient to have his sputum examined as much as it will harm the reputations of some of us to omit it. In many doubtful cases the occurrence of tubercle bacilli in the sputum alone settles the diagnosis. The great emphasis laid upon the occurrence of pulmonary tuberculosis without

tubercle bacilli in the sputum has led in some instances to a neglect of this most important procedure. Tubercle bacilli are often lacking early in the disease when their presence would help us most, and I have seen several cases in which only after extensive involvement of the lung, and only a comparatively short time before death, were tubercle bacilli found in the sputum. Curiously enough the disease may advance in rare instances with little if any increase of symptoms and practically no sputum containing tubercle bacilli. It is of interest to note that in many advanced chronic non-tuberculous pulmonary diseases the chief if not the only point of differentiation is the absence of tubercle bacilli in the sputum. Tubercle bacilli, as you are aware, may be found in the feces and in the stomach content when no sputum can be obtained for examination.

Rales rank next in diagnostic importance to the presence of tubercle bacilli in the sputum. While rales of any description, whether crepitant, fine, moderately coarse, coarse or sonorous or sibilant rhonchi, may and often do, occur in pulmonary tuberculosis, the rale usual in incipient tuberculosis is a moderately coarse rale, depending for resonancy or dulness upon the amount of solidification of pulmonary tissue between the bronchiole or bronchus and the chest wall, heard often only during the rather hurried, somewhat full inspiration that follows a cough. I shall not dwell upon the importance of using a cough in physical examination, for even Laennec called attention to the fact that rales were better heard under such conditions. If after cough you hear no rale be sure to have your patient breathe out half or nearly all of his breath, then cough and inhale as I have indicated. I am sure that all of you are familiar with this procedure. I would like to emphasize, however, one point. Throughout the whole physical examination, and particularly while he is coughing, see that all the muscles are relaxed. If you do not observe this precaution you may overlook rales that are numerous throughout the chest. Too hard a cough may also defeat your purpose. If such rales as I have mentioned are heard in quiet respiration the case has always, in my experience, passed beyond the incipient stage.

The physical examination of the patient has assumed today with the perfection of roentgen-ray technic a position of greater interest and of no less value. The frequency with which tuberculosis early in its course attacks the pulmonary apices, which are, of course, comparatively small in extent and readily susceptible to examination has given physical examination in pulmonary tuberculosis an importance vastly greater for example, than in pulmonary abscess, where extensive pulmonitis may exist about an abscess cavity in the upper or lower lobes, and yet the only physical signs may be some slight change on percussion and distant breathing. It is indeed fortunate for patients that pulmonary tuberculosis so rarely arises and remains localized in the more central parts of the lungs.

However, whatever part of the lung is usually first affected the physical signs most frequently appear first at the apex.

Now the rale to be of significance must occur in the upper part of the lung and must be constant on several examinations. Such apical rales are of greater moment when heard posteriorly to the third vertebral spine than when they occur above the clavicle and in the first intercostal space. Typical rales in a suspicious case rank high in diagnostic import; next, I might repeat, to the tubercle bacilli.

There can be no question that pulmonary tuberculosis can occur without rales, and, indeed, fairly extensive deep-seated disease may exist without any or only with most indefinite physical signs. Symptoms may force a diagnosis of pulmonary tuberculosis, and tubercle bacilli may even be found in the sputum and still no abnormal physical signs occur. It is a common occurrence, I am sure, for many of you to find with a right apical lesion typical rales in the outer fourth and fifth intercostal spaces on the left. These are caused by a deep-seated bronchogenic spread of the disease to the other side. Cases do occur in which only indefinite signs are to be heard for some time, and then suddenly rales appear in an unusual situation and may quickly spread over the whole side. Again I have noticed that as the rales increase some patients become better in every way. The deep-seated disease then may approach finally and quickly the surface of the lung, or at least the bronchi within the area susceptible to stethoscopic investigation contain suddenly an abnormal amount of secretion.

Rales when heard only at the base of one or both lungs should never be considered as due to pulmonary tuberculosis unless tubercle bacilli are present.

Granular breathing, that type of breathing which seems about to break up into fine rales, which suggests that with a cough, rales will be plainly evident (when possibly they may not occur), distant breathing at the right apex, prolonged expiration, possibly high-pitched at the right apex, or high-pitched inspiration, with some roughening or accentuation at the left apex, are among the slighter signs to be carefully noted.

The extensive use of the roentgen ray has been a godsend to many men condemned through ill health to pass their days listening to lungs affected with pulmonary tuberculosis, which through force of circumstances they can never follow to and examine at the end. Here they have a means of repeated autopsies or "shadow biopsies," if I may employ the term. Even if they do fail to reveal some tuberculosis, although in some hands they may be grossly misinterpreted, they have added greatly to the efficiency and accuracy of diagnosis. Take an hour or two off occasionally when you have to go to the radiographer's, and follow him in his interpretation of your plates and others. It is a technic that is just as important for you as that of the laryngoscope or of the ophthalmoscope. I

have no time tonight to go into the details of roentgen-ray diagnosis of pulmonary tuberculosis, but I desire to mention a few of the conclusions that I have reached after prolonged use of roentgen-ray methods.

In the first place you will be asked when you report your patient to the board of health, if he has incipient, moderately advanced or far-advanced pulmonary tuberculosis. This is also required by many institutions if you wish to enter him therein. I am convinced from my observations of the comparisons of many physical examinations and roentgen-ray plates that in a very large majority of cases the roentgen ray shows much more disease than is revealed by physical signs. Recently I have been impressed with the idea that we should replace the term "incipient" by the term "minimal," which implies nothing in regard to time, and everything that we wish in regard to early diagnosis. I have mentioned this for I believe the time is coming when to decide that a patient is really in the minimal stage, roentgen rays must be used, for they show, as I have said, that many of the cases called today "incipient" are really moderately advanced, for we can examine by physical signs only the peripheral portion of the lungs, and unless disease involves this portion it may entirely escape our notice.

In the second place you may be suspicious, on account of slight respiratory changes of an apex, and in no cases does the roentgen ray help more than in these truly minimal cases, where it may reveal a well-marked more or less deeply seated parenchymatous lesion and decide the diagnosis.

In the third place roentgen-ray examination may reveal that the abnormal physical signs are due not to tuberculosis but to some other cause.

I will not pursue this point further but must emphasize that not every radiographer can take plates of the chest suitable for pulmonary diagnosis, and, further, may at times draw conclusions from faulty or excellent plates that seem to me entirely untenable. However this may be, I believe that suspicious symptoms demand not only a carefuly physical examination, but a roentgenologic study as well.

Our statistics at Trudeau have been very carefully studied from time to time by Doctor Heise and by some of the rest of us. He has emphasized the importance in diagnosis of two points in the past history of the patient: I refer to the occurrence of hemoptysis, and of pleurisy, which is of more import if associated with effusion. The hemoptysis, of course, must be a dram or more, and is more important diagnostically if followed by streaked sputum for a day or two, or, indeed, if the hemoptysis recurs once or twice. I do not mean to say that streaked sputum is of no moment, for it may be the signboard that suggests the direction of the diagnostic goal. But it does occur frequently in acute bronchitis, and all of you are

aware of the occurrence of frank hemoptysis in pulmonary abscess and more rarely in bronchiectasis.

If our patient has had one of these symptoms we must not only suspect but exclude pulmonary tuberculosis.

I cannot but feel that in all tuberculous pleurisies, with or without effusion, the tuberculosis has gained entrance to the pleura through the blood or lymph vessels of the lung. It is now well known that many small lymph glands and masses of lymphoid tissue are scattered practically throughout the lung, and it is difficult to believe that some tubercle bacilli may not remain behind in some of these lymphoid masses. The experimental work of Patterson and others has proved that tuberculous pleurisy with effusion is always secondary to some other tuberculous focus in the body. In other words, it is the reaction of a sensitized pleura to renewed irritation by the sensitizing agent. It needs but a moment's reflection to conclude that any focus in the body that is shedding tubercle bacilli into the circulation needs our attention at once and demands from us discovery of its location if possible, and in any case careful treatment.

The laboratory furnishes us with many valuable aids, and makes, as I have said, by the discovery of tubercle bacilli, the only diagnosis that is absolutely unquestionable. The importance of the tuberculin cutaneous test in the first few years of life is known to all of you, but in adults no cutaneous, ophthalmic or subcutaneous reaction separates in my opinion active from inactive tuberculosis, or tuberculosis that needs no care from that which demands active treatment. The complement-fixation is positive in the majority of cases, but the fact that 10 per cent. of the patients with tubercle bacilli in the sputum fail to react positively weakens its diagnostic value. It is much like the Widal reaction in typhoid or the Wassermann reaction in syphilis. The clinical data are more important. The repeated absence of a positive complement-fixation test, however, in a case that is only doubtfully tuberculous, and in a moderately advanced stage of disease, lends considerable weight to a diagnosis of non-tuberculous disease.

The determination of the presence of pulmonary tuberculosis does not complete the diagnosis. A positive cutaneous tuberculin test reveals that the patient is allergic and has harbored tubercle bacilli for a time at least in his body. The occurrence of the two symptoms I have emphasized, the presence of abnormal physical signs mentioned, confirmatory roentgen-ray findings decide the presence of pulmonary tuberculosis, even in the absence of tubercle bacilli in the sputum. But here we must solve what is for the patient the crucial point—does he need treatment? In some cases with slight physical and roentgen-ray changes in the lungs we have employed the subcutaneous tuberculin test and studied the lungs for a focal reaction, which occurred in about 18 per cent. when the test was

positive. In all we have given 324 patients the subcutaneous test. Of these 10 have died of tuberculosis and 59 have relapsed in a period covering from two to eighteen or twenty years. In other words, 25 per cent. in whom we were not sure of a diagnosis relapsed and 4 per cent. have died. Of the 42 patients who have failed to react to a second dose of 10 mg. of Old Tuberculin, 2 have relapsed and recovered and 2 have died, 1 from acute lobar pneumonia and 1 from a cause unknown.

As I have come to learn what an amount of disease a chest may contain when the physical signs are equivocal, I wonder that one of these 282 patients were not permanently injured after sharp reactions; but, on the contrary, many felt better, and asked for this reason to be given tuberculin as a treatment. Today we take no such chances, and if the roentgen ray shows any parenchymatous changes they must be very indefinite or else very old and calcified. In our recent cases (numbering 30) we have had 4 only that showed a definite increase of clouding about the suspected areas, and in some of them rales occurred for the first time. Today we send home at once a patient who fails to react to two doses of 10 mg. If he reacts and still shows no change by physical signs or in roentgen ray, we increase rapidly his exercise and send him home in a few weeks if he does well. None of the 42 has ever reapplied for admission, though we have always told them we would take them in at once if they relapsed.

Only a small number of patients can be submitted to such tests, and for many the problem of whether the disease under consideration is active or inactive is not easily solved. We have made some study of it and have attempted to divide the symptoms in relation to activity into two groups: (1) Cardinal symptoms, including hemoptysis, pleurisy, fever, rapid pulse, lack of endurance, loss of weight and night-sweats, and (2) subsidiary symptoms, including chills, cough and expectoration. In our studies we have not considered the presence of tubercle bacilli in the sputum as evidence of clinical activity, though we realize that such patients are much more likely to relapse. We have arbitrarily chosen a temperature of 99° F. in the male adult and 99.5° in the female, and a pulse-rate of 90 in a male and 96 in a female as the upper limits in non-active cases. Of course, other disturbing factors must be excluded. We studied 198 patients in regard to relapse and found that 90 per cent. of the relapsed had a positive complement-fixation test and that 70 per cent. had been considered "clinically active," while of those who did not relapse 50 per cent. had a positive complement-fixation test and 75 per cent. were "clinically active." The presence of rales was not of much help, and even when they occurred, with tubercle bacilli in the sputum, only 50 per cent. were considered clinically active. The whole subject is very intricate and needs further study, as you can readily see from these figures.

To summarize briefly I feel that fever, rapid pulse, lack of endurance, loss of weight and night-sweats suggest tuberculosis which must be excluded if possible. If to these we add cough and expectoration, which have persisted for several weeks, we must focus our attention for a time on the lungs. But if we can find no more evidence than the symptoms I have just mentioned I do not feel that we can make an absolute diagnosis of pulmonary tuberculosis. To do so one or more of the six diagnostic essentials that I stated in a negative way a few minutes ago must be present. I refer to tubercle bacilli in the sputum (confirmed on two examinations); persistent moderately coarse rales in the upper chest; a parenchymatous roentgen-ray lesion, more weighty if in the upper chest; a history of frank hemoptysis, of pleurisy and a positive complement-fixation test.

Tubercle bacilli, of course, settle the diagnosis. Moderately coarse rales persistent at an apex, more particularly if posteriorly, are nearly as positive as tubercle bacilli unless due to some acute process in the course of clearing up, and then they fail to be persistent. A parenchymatous lesion, more especially in the upper part of the lung, if we can exclude influenza and some of the epidemics seen in the army, ranks a little below the rales described. A combination of rales and a parenchymatous lesion is, of course, more certain than either alone. If to these we can add a history of hemoptysis or pleurisy with effusion the diagnosis can be considered positive. I am speaking now of cases in which tubercle bacilli have never been found. A history of hemoptysis or pleurisy with effusion which cannot be explained by any other cause, in spite of the absence of tubercle bacilli, rales or definite roentgen-ray picture, demands a diagnosis of suspected pulmonary tuberculosis.

The combination of a positive history for hemoptysis or pleurisy with either rales or parenchymatous roentgen-ray lesions demands a positive diagnosis under the conditions mentioned above. A negative complement-fixation test in a patient with moderately advanced disease, without tubercle bacilli in the sputum, bespeaks caution in making a definite diagnosis of pulmonary tuberculosis.

Treatment.—Having made a diagnosis of pulmonary tuberculosis and having satisfied yourself that the case needs vigorous treatment, the next step is most important. Pulmonary tuberculosis is a chronic disease. If we exclude miliary tuberculosis, for which there is no treatment with cure as an outcome, even the more acute cases rarely die in less than six months, and, as is well known, the average duration of all fatal cases is between two and three years. The struggle for recovery lasts no shorter time, and if we include relapses, or "setbacks," as our patients call them, extends over a far longer period. In fact, I feel that with many patients the struggle lasts from diagnosis to death, which in at least 90 per cent. of the patients at Trudeau has been caused by tuberculosis.

It is easy to deduce from these facts that a physician must have a sanguine temperament to deal successfully with such a disease, for patient, family and friends all lose courage and grow despondent over the many disappointments that beset the path toward recovery.

Bearing these facts in mind the psychologic treatment of the patient demands careful thought. I do not believe it pays to temporize with the patient. He should be told at once that he has pulmonary tuberculosis. It may come as a shock and nearly prostrate the patient for a while, but you will be the gainer, and in the end the patient will be benefited. He does not and cannot know the difficulties ahead of him, and I doubt the advisability of emphasizing them too much at first. But be sure to tell him enough to gain his whole-souled coöperation. Awake in him, if you can, a fighting spirit. Encourage him or depress him or do both, but from the minute you tell him of the diagnosis assume a strict attitude toward what he should do.

This leads me to emphasize the benefits that many patients derive from proper treatment at its onset, and to call to your attention the "danger time" that the patient passes through at the outset of treatment. I refer to the period of time, usually several weeks, during which the education of the patient progresses to a point where he becomes orientated and aware of the many dangers that follow overexertion. I know of no way more certain to avoid these dangers than to keep your patient in bed on a porch or in a room with wide-open windows until his education has progressed to a point that you feel you can trust him not to overdo. Tell him that he has specks on his lungs like those that occur in apples in March, and that while the apple must necessarily decay in order to liberate the seeds, his lung is constantly forming delicate scar tissue about these specks or tubercles which contain the germs, in an endeavor to wall them off, and, so to speak, strangle the germ in its own juices or excretions. Tell him that at first the scar tissue is so delicate that it resembles spider web and that vigorous or violent respiratory exertions may stretch the delicate scar, liberate some germs which may form new specks or spots which in turn will have to be walled off before he can hope for recovery. In short, say to him that the treatment of pulmonary tuberculosis depends upon two things: (1) the formation of scar tissue, and (2) the protection of the forming scar tissue. The conservation of energy and the conservation of natural resources are familiar to many patients. Tell them rest enables their body to devote more of its powers to form scar tissue and rest of the lungs protects the delicate scars. I try to illustrate this point with my hands.

In recent years I have come to regard rest as the most important point in the treatment of pulmonary tuberculosis. It is far better for a patient to be in bed in a room with fair ventilation for several weeks than to dress and to walk some blocks to a park where he

can sit out for several hours and climb several flights of stairs to regain his room. If you can persuade your patient to do this, seize upon the opportunity to educate him. Put such literature in his hands as he can comprehend and encourage him to write down questions. Tell him frankly that your visits are as important educationally as medically. If you can get him to think out his problem, three-fourths of the battle is won. I usually try to keep my afebrile patients in bed six weeks. Patients with fever demand much longer periods of rest.

Exercise at the proper time is as important as rest, but even then vastly more dangerous. The scar, of course, at the end of six weeks is not densely fibrous and requires careful stretching, such as is exerted by gentle breathing. I do not refer to respiratory exercises, which I seldom use. To reëducate the patient physically requires that the physician should become a physical trainer, who never forgets that he is dealing with a damaged organ that demands far more rest than a normal organ. This, too, must be impressed upon the patient. I sometimes put it that they can play and get well or work and get well, but they cannot work and play and get well. To watch the effect of any new form of exercise, have your patients take it every other day. It has seemed to me that afebrile patients kept in bed six weeks could be given exercise rather quickly. I frequently allow them to take, after they are accustomed to dressing, to going to meals and to climbing the necessary flight of stairs, one-quarter of an hour's slow walking twice a day the first week, one-half the second, three-quarters the third, and one hour the fourth provided, of course, there has been no increase of symptoms. After that if I feel that I can trust the patient I put him on unlimited exercise and tell him never to get out of breath or to get tired. Of course, many patients do not advance this rapidly, and remain at fifteen to thirty minutes twice daily for some weeks. Such treatment as I have just outlined is applicable only to early and favorable cases.

Since the first century of the present era, and possibly before, air or climate has been extolled in the treatment of pulmonary tuberculosis. The oxygen of the air enters the body through the lungs. So air is necessary to the lungs, it has been argued, and bad air would therefore affect the lungs deleteriously. Hence the value of good air for the diseased lungs. Curiously enough the lungs can use and do well in air in which a man cannot live. The value of live, fresh air lies not in its effect upon the lungs, but through the effect upon the body in general. It affects the lungs no more, no less, than the knee. The value of air is exerted in what might be called the air bath. I refer to having fresh air circulate about the patient. It is better, of course, to have him out of doors, but, as I have already said, it is better to be indoors with open windows than overexercising to get fresh air. Window tents that expose the head and neck while

the body is in a warm and possibly badly ventilated room produce the same effect in pulmonary tuberculosis as spraying the face and neck in typhoid fever. Both are good as far as they go, but they stop short of the essential.

Food requirements in pulmonary tuberculosis have undergone considerable change. At first the patient was overfed and now we realize that food has a specific object in this treatment and should be prescribed accordingly. The struggle against pulmonary tuberculosis is a fight to strengthen and to build up the recuperative powers within the individual patients. Scar tissue must be formed. Calcium salts must be deposited. The increased wear and tear of fever, which increases the caloric output of the body by 50 per cent., must be combated. At the same time such patients crave little food. The old idea was that patients needed much meat and milk. It is of interest to note that when after the war an attempt was made to put flesh on some Germans by greatly increasing their fats and carbohydrates it could not be done until an excess of meat was added to the diet. It seems that extra meat is necessary until the patient has a proper amount of protein in his body. If excess of calcium salts are necessary no food furnishes such an amount of this dietary essential as milk, combined, too, probably in such a way that it can be used at once by the body. The fact that the calcium content of the blood serum does not vary in pulmonary tuberculosis is no argument in my mind against its use. One may recall that the same argument was used against the use of iron salts in anemia. Is it not possible that with an increased amount of calcium in the food the blood may pass on to the tissues or scar formation an increased amount of calcium? With a judicious use of milk there is no call for any anxiety about a lack of fat-soluble in the diet of our patients, but it is of interest to note that cod-liver oil and butter fats contain it in large quantities, while all vegetable oils and fats are deficient in it or lack it entirely. The water-soluble B is practically always supplied in sufficient quantities.

In concluding, I should like to state that not every patient in whom a diagnosis of pulmonary tuberculosis can be made needs vigorous treatment. It was an attempt to discover some simple method that any practitioner could use in his office that led us to begin our study of active and inactive cases. We found no simple method. However, my impressions have led me to believe that in considering the need for treatment, symptoms vastly outweigh physical findings in the majority of cases. I frequently tell my patients that the signs the doctor discovers are like the green lights on the railroad, while the symptoms from which they suffer are red lights. A green light means run carefully, and a red light means stop or go on the side track. Tubercle bacilli can, of course, occur in a perfectly quiescent case, that needs follow only a careful life, but when it occurs in a patient who has but recently begun to have

symptoms, vigorous treatment is demanded. Rales, of course, can persist for years in arrested cases. I have seen them apparently unchanged after ten years. The roentgen ray helps greatly in revealing changes that occur from time to time, not discoverable by ordinary methods of physical exploration. But do not forget that an increase of roentgen-ray shadows may occur months before the last plate has been taken, and at that time the patient may have arrested his disease.

Any patient with unexplained pleurisy with effusion needs treatment for pulmonary tuberculosis unless you can exclude definitely any parenchymatous lesion in his lungs, and even then I should incline to the side of caution, for a slight deposit may be lost in the cloudiness that obscures the plate in part at least. An inexplicable hemoptysis should be similarly treated.

Suspected pulmonary tuberculosis we treat by rapidly increasing the patient's exercise to the unlimited stage, and after about three months, if all has gone well, return him to his work.

Finally, we believe that after a careful study the patient can be taken into confidence and frankly told the possibilities—presupposing, of course, that he has some intelligence. Otherwise your final decision must be meted out to him in no doubtful language.

ENDOTHELIAL LEUKOCYTES IN THE URINE SUGGESTING TYPHOID INFECTION.

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Several years ago I reported in this journal[1] a case in which the diagnosis of acute pleurisy with effusion, due to the Bacillus typhosus, was arrived at through the finding of endothelial phagocytes in the fluid obtained by pleural puncture. The diagnosis was verified by obtaining from the pleural fluid a pure culture of Bacillus typhosus and by the demonstration that both the pleural fluid and the patient's blood serum produced agglutination of known typhoid bacilli.

In the present instance the case to be reported has this point of similarity: that the diagnosis of infection with the typhoid bacillus was reached as a result of the finding of numerous cells which closely resembled the endothelial leukocytes so regularly seen in the various lesions of typhoid fever. In the present instance these cells were found in the urine.

The constancy of the reaction of endothelial leukocytes, using this term in the sense in which it is employed by Mallory, to the

[1] Am. Jour. Med. Sc., 1916, cli, 663.

toxin of the typhoid bacillus, is so marked as to raise a suspicion that the typhoid bacillus is the probable etiologic factor in any cellular reaction in which the endothelial leukocyte predominates, no matter in what portion of the body this occurs. Of course, it must be remembered that the typhoid bacillus is by no means the only organism which brings about an endothelial reaction. Nor is the active phagocytosis displayed by endothelial leukocytes in typhoid lesions peculiar to that infection, although the phagocytic activity may be more marked in typhoid fever than in tuberculosis or in the other conditions in which an endothelial reaction occurs. Furthermore, we must remember that the number and type of cells engulfed by the endothelial leukocytes varies in different regions with the supply and character of cells at hand to be phagocytized.

The observation here recorded may be additional evidence of the universality of the reaction to the typhoid bacillus and of its possible value in the recognition of unsuspected infection with this organism. No more positive claim can be made because of the uncertainty concerning the nature of the cells found in the urine.

The case to be reported is that of a patient who was on the surgical service of the Hospital of the University of Pennsylvania, under the care of Dr. A. C. Wood, by whose courtesy I was permitted to study the case and to make this report.

Case History. The patient, a boy, aged sixteen years, was admitted to the hospital on November 7, 1919. His chief complaint was pain in the lumbar region. The history, which was difficult to elicit, and is probably incomplete, was given as follows: On July 4, 1919, the patient took sick and was forced to go to bed. The only symptoms the patient can recall were fever and frequent, painful micturition. The doctor who was called made no diagnosis to the patient's knowledge. The illness kept him in bed for fifteen days, and he was confined to the house for a month.

Subsequent to the illness a pain developed in the left lumbar region which was localized, deep-seated and aggravated by motion. It also seemed to be worse at night, keeping him awake. There were remissions in the pain at first, but after two-and-a-half months, as a result of lifting a heavy weight, the pain became worse and seemed to involve the lumbar spine. Again improvement took place, until six weeks before admission, while playing leap-frog one of his playmates fell upon his back. This aggravated the pain and he was taken to a hospital, where a diagnosis of curvature of the spine was made and he was sent to the University Hospital for treatment.

Since the onset of his present illness he has been somewhat constipated and has had gaseous eructations. His appetite has been poor and he has lost some weight. He has always been a little short of breath and has had palpitation. He did not complain upon admission of any urinary symptoms.

His previous medical history is negative, except for influenza in October, 1918. No venereal infection admitted. He works in a tannery, sorting leather. Otherwise his social history is unimportant. Family history negative.

Physical examination on admission was recorded as negative except for the following statement: "Tenderness alongside the lumbar vertebræ in the muscles. Vertebræ not tender to pressure. Some disinclination to bending spine. Pain also on pressure under left costal margin." On the day of admission the laboratory examinations were: Urine: amber; cloudy; flocculent sediment; specific gravity, 1015; albumin negative; sugar negative. Microscopically: casts negative; cylindroids negative; mucus + +; red blood cells, negative; white blood cells, 1 or 2; epithelium +; triple phosphate crystals.

Blood: Red blood cells, 4,510,000; hemoglobin, 62 per cent.; white blood cells, 9900. Differential count: Neutrophiles, 66 per cent.; lymphocytes, 25 per cent.; large mononuclears, 4 per cent.; transitionals, 2 per cent.; eosinophiles, 2 per cent.; basophiles, 1 per cent.

The following ward notes were made.

November 8. Patient complains of more pain in the left side and the back.

November 9. Pain obviously worse; each breath causes pain, and there is some cough. Examination revealed the spinal muscles on both sides in spasm. The right side of the back over the right kidney is markedly fuller than the left. There is impairment to percussion over the base of the right lung, but not much change in the character of the breath sounds.

Temperature has risen to 102°, pulse, 120; respirations, 28.

November 10. Condition unchanged. Temperature fell to normal in morning up to 102.4° by night. Pulse, 112. Respirations, 24.

The patient continued to complain of severe pain and to run an irregular fever, with moderate acceleration of pulse and respiration.

November 13. Leukocyte count, 8000.

November 17. Leukocyte count, 8800. Polymorphonuclears, 57 per cent.; lymphocytes, 35 per cent.; eosinophiles, 3 per cent.

On November 18 I was first asked to examine the patient. The fever and the pain in the back were still the prominent features of the case and physical examination was negative except for the discovery of slight impairment to percussion at the right base posteriorly, with a few faint frictions or rales, but no change in breath sounds. There was tenderness in the iliocostal space on the left side and apparently some spasm of the spinal muscles in this region. An urticaria, probably due to medication, was also present.

A specimen of urine was obtained and found to be grossly cloudy. Centrifugation threw down a whitish sediment resembling pus, but on microscopic examination I found it consisted not of the expected

pus cells but of larger cells, many very large and vacuolated. Their cytoplasm was stained faintly by methylene blue, and, as a rule, there was one large nucleus, though a few cells were seen, with two distinct nuclei. The vacuoles were not present in every cell and varied in number and size. In addition to the vacuoles there were seen in many of the cells round areas of homogeneous appearance resembling fat or hyalin. Some of these took a greenish tint with the methylene blue; none took the fat stains. In a few instances the large cells seemed to contain remnants of lymphocytes, but this was uncertain. It must be remembered that the endothelial leukocytes engulf a variety of cells under different circumstances. In this instance there were apparently no erythrocytes and few other cells available, as no erythrocytes or leukocytes were found in the urine.

The appearance of the large cells strongly suggested phagocytic endothelial leukocytes, and although no suspicion of typhoid infection had been entertained, and the suggestion that these cells might indicate typhoid infection was not taken very seriously, yet it was deemed significant enough for an agglutination test and a culture of the urine to be requested from the laboratory. The report of a positive agglutination test was received, which was, it must be admitted, unexpected. The patient's serum was then sent a second time to the laboratory and was again found to agglutinate the Bacillus typhosus in the usual dilutions, while with paratyphosus beta there was only slight agglutination and with alpha none at all. Two urinary cultures were negative, but from a third culture a free growth of Bacillus typhosus was obtained. This also was confirmed by a fourth examination.

November 19. The patient was better and the temperature lower and the signs at the right base were less marked. The urine no longer showed the large cells seen the previous day, but instead a few clumps of polymorphonuclear leukocytes.

November 20. A fluoroscopic examination revealed no lung pathology and no evidence of subdiaphragmatic abscess. The temperature was normal all day; pulse and respiration about normal.

November 21. The patient was better and had less pain. Signs at the right base had wholly disappeared.

Phenolsulphonephthalein elimination: 50 per cent. in two hours.

November 24. Patient much better. Temperature below 99°. Still complained of pain at night, which was now exclusively on the right side. Tenderness posteriorly was much diminished and there was none anteriorly.

Patient continued to improve and exhibited no new symptoms.

Discussion. There are many points in the report concerning which one would wish more information. It is, of course, impossible to be certain at what time the patient acquired the typhoid bacillus infection. It seems most probable that the febrile attack in July was true typhoid fever, since it was the only febrile illness in his

history, and since the possibility of catheter infection can be excluded also. Another important question which cannot be answered concerns the relationship between the symptoms of which the patient complained following the febrile attack in July and the occurrence of typhoid bacilli in his urine. If the patient was a urinary carrier it is difficult to explain the symptoms, for the carrier state is unfortunately peculiarly lacking in symptoms except in those carriers in whom there is sufficient gall-bladder trouble to attract attention. Whether "typhoid spine" may occur in carriers or bear any relation to the carrier state is unknown. Nor did this patient's symptoms agree entirely with the picture of "typhoid spine."

On the other hand the urinary findings in this case are not those of actual infection of the urinary tract with the typhoid bacillus. The typhoid bacillus may produce cystitis, pyelitis, pyonephrosis and even an acute urethritis, but in all these instances there is a pyuria in which the usual polymorphonuclear neutrophile predominates. No such pyuria was observed in this patient. A search of the literature reveals no statement as to the cellular elements in the urine of urinary typhoid carriers nor any description of the occurrence of phagocytic endothelial cells, although there seems no good reason why these cells should not reach the urine, as they are found in tubular nephritis lying free in the urinary tubules busily engulfing necrotic epithelial cells.

There is still doubt as to the origin of the typhoid bacilli found in urinary carriers, and the direct relation of gall-bladder infection needs further demonstration. The possibility of foci in the urinary bladder or even in the kidney has not been excluded nor has the possibility that under certain conditions, such as perhaps trauma or secondary infection, the quiescent foci of the carrier state might be transfromed into active infection of the urinary tract. It is remotely possible that this case was an example of this kind.

Aside from these speculations, which are bound to be inconclusive, the fact remains that in this instance a most unusual cellular picture in the urine was observed, and, whether rightly or wrongly, a line of reasoning was followed which led to the discovery of typhoid bacilli in the patient's urine and of a positive Widal test in the blood serum.

This experience suggests that something may be learned from the study of the cells in the urine of urinary typhoid carriers, and that the recognition of endothelial leukocytes in the urine may be helpful diagnostically.

A CONSIDERATION OF CERTAIN ASPECTS OF PROTEIN HYPERSENSITIVENESS IN CHILDREN.

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At the present time it is not unusual to see infants and children who are hypersensitive to proteins and who manifest their sensitiveness by a number of different clinical symptoms. Nearly everyone knows of individuals who are made ill, regularly, after eating fruit or shell-fish, or who are unable to come closely in contact with animals or grasses without developing hay fever or asthma. This idiosyncrasy or susceptibility to various substances has been recognized for a long time. Among the earlier medical writings on this subject are those of Elliotson,[1] Hutchinson[2] and Blackley.[3] Elliotson drew attention, in 1831, to the association between the pollen of plants and hay fever while Blackley, in 1873, not only recognized this association but produced edema and congestion of the conjunctiva by the instillation of certain pollens in the eyes of hay-fever patients. He also observed that the pollens produced an area of edema and erythema when rubbed into the abraded skin of such patients. In 1884 Hutchinson referred to a number of patients who complained of nausea, vomiting and abdominal discomfort, and he believed these symptoms were due to the eating of egg, as the symptoms disappeared when egg was withheld from the diet. He stated also that certain individuals might be susceptible to other articles of food, such as honey, tea, coffee and different fruits and vegetables.

The more common and characteristic features of hypersensitiveness to proteins, which occur in infants and children, are shown by the following case reports:

Case I.—An infant, who had been exclusively breast-fed, was given, when six weeks old, a small amount of cows' milk. This was immediately vomited. One month later one-half teaspoonful of milk caused a severe general reaction. The baby vomited and had diarrhea. He became cyanosed and so prostrated that the physician considered him dangerously ill. Bread prepared with cows' milk brought on a similar reaction, as did the administration of three drops of a 1 in 12 dilution of condensed milk. Cows' milk in any form and in infinitesimal amounts always caused vomiting, loose stools, cyanosis, irregular respirations and prostration. He

[1] Clinical Lecture, March 31, 1831, Lancet, 1830–31, xx, 370.
[2] The Pedigree of Disease, p. 28.
[3] Experimental Researches on the Cause and Nature of Hay Fever, London, 1873.

was able to take goats' milk without any symptoms. In order to determine that the symptoms were due to cows' milk the protein of cows' milk was applied to the skin. This was followed by an area of edema and erythema after four hours. When introduced in this manner cows' milk caused the same general symptoms as when taken by mouth. Protein from beef, egg, horse serum, barley, human milk and goats' milk caused no reaction when applied to the skin. The baby was nursed at the breast and given supplemental feedings of goat's milk until ten months old, after which minute amounts of cows' milk was given by mouth. Gradually the amount was increased until the hypersensitiveness to cows' milk was overcome. The paternal aunt had an idiosyncrasy to shellfish and the paternal grandfather and great-grandfather had asthma.

Case II.—An infant, aged two years, was breast-fed for two months, after which he was given a formula of cows' milk. Cereals, broths and vegetables were added subsequently. Eczema appeared when he was one month old, and it had been persistent. When one year old he was given a soft-boiled egg. This was immediately vomited and he was sick for several hours. Six months later egg was given and he again vomited. The protein of egg, cows' milk, barley, horse serum and beef gave a marked reaction when applied to the skin. By omitting eggs, meats and milk from the diet the eczema improved, and by giving them in small amounts and gradually increasing them he was finally able to take these foods without a return of the eczema. The mother had eczema when she was an infant.

Case III.—The patient, a girl, aged four and a half years, was breast-fed until she was ten months old. When eight months old an egg shampoo caused a severe urticaria of the head and face. About the same time the eating of a teaspoonful of custard caused a generalized urticaria, with marked swelling about the mouth. When twenty-two months old she became violently ill following the eating of custard, and was thought to have "ptomain poisoning." It was not realized at this time that the symptoms were caused by egg. Urticaria always followed the ingestion of egg in any form. Urticaria also followed the eating of peanuts and walnuts. The protein of egg was rubbed on the skin and a huge urticarial-like wheal appeared immediately. After forty-five minutes urticaria appeared all over the body and the eyes, ears, lips and vulva became swollen and red. The patient became nauseated and complained of abdominal pain and faintness. This patient has not been treated for hypersensitiveness to egg. A maternal aunt was sensitive to egg.

Case IV.—The patient, aged four years, was given a small amount of egg when eight months old. She vomited immediately and had a generalized urticaria. Subsequently she was able to take egg in the small amount contained in cakes and pastry. When

eighteen months old asthma began. When the protein of egg was applied to the skin a huge urticarial-like wheal appeared. Egg and foodstuffs containing egg were excluded from the diet and she remained free from asthma for a year. Asthma then recurred. The protein of a number of different substances was applied to the skin and very definite positive reactions to cows' milk and beef were found. When egg, milk and meats were withheld the patient did not have asthma.

CASE V.—This patient was nine years old. When two years of age eczema appeared for the first time and persisted for four years. After that urticaria appeared and the eczema improved but did not entirely disappear. When eight years of age asthmatic attacks began and they recurred at rather frequent intervals afterward. It is interesting that the ingestion of cereals always caused a swelling of the mucous membranes of the mouth, which was accompanied by severe itching about the mouth. The protein of egg, beef, milk, oatmeal, barley and wheatena caused marked edema and erythema when applied to the skin. This patient is now undergoing treatment for hypersensitiveness to protein. A maternal aunt has asthma and the maternal grandmother has hay fever.

CASE VI.—The patient, aged ten years, was breast-fed four months and then weaned on account of a severe and extensive eczema. After the first year the eczema was less severe, but it persisted, and at the time of admission to the hospital, eczema involved the face, the flexor surfaces of the arms and the scrotum. Many different forms of treatment had been tried unsuccessfully. The sensitiveness to proteins was observed when six months old, when he was first given egg. Egg, fish and nuts always intensified the eczema, and the eating of any of them was followed almost immediately by a burning sensation in the throat, vomiting, diarrhea, edema of the lips and ears and urticaria. In addition to these manifestations, association with horses always causes urticaria and hay fever. A marked reaction of the skin was obtained with the protein of milk, egg, horse serum and horse dander. The patient was relieved by withholding egg, milk and meats from the diet, and, after being desensitized to them, has had no return of the symptoms.

Within the past few years much information relating to the nature of the symptoms, which are caused when a sensitive person comes in contact with various substances, has been obtained.[4] It has been established definitely that the symptoms in these cases

[4] The reader is referred to the articles by the following writers who have contributed largely to this subject and from which I have quoted freely: Schloss, O. M.: Am. Jour. Dis. Children, iii, 341. Talbot: Boston Med. and Surg. Jour., 1914, xlxxi, 708. Longcope, W. T.: Harvey Lecture, 1915–16, p. 271. Cooke, Robert A., and Vander Veer, Albert: Jour. Immun., i, 201. Walker, Chandler: Oxford Medicine ii, 115. Rackemann, F. M.: Boston Med. and Surg. Jour., 178, 770. Kolmer Infection, Immunity and Specific Therapy, second edition, p. 614.

are due to protein which is contained in the substances to which the patients react.

In many ways human sensitization, as it is generally termed, is analogous to the anaphylactic reaction in animals. There is a close similarity between many of the clinical manifestations observed in man and those seen in anaphylactic shock in animals. The specific skin sensitiveness in animals and the skin reaction observed in serum disease closely resemble the protein skin reaction, which constitutes an important feature is the condition under discussion.

It is not necessary in this communication to give in detail the many experiments which have been undertaken to demonstrate a relationship between human sensitization and experimental anaphylaxis in animals. Human sensitization is not identical with the artificial sensitization with antitoxin sera or with experimental anaphylaxis in animals. They differ in certain respects, and definite conclusions should not be drawn until these differences have been subjected to more careful experimental investigation.

The hypersensitive state may be present at birth, and this is the rule in a large percentage of the cases, so that severe and even alarming manifestations result at the primary contact with the protein. In the case reported by Park,[5] vomiting and diarrhea and cyanosis and prostration were induced when the infant received for the first time only a small amount of cows' milk. Less severe manifestations, as eczema, urticaria and asthma, may develop as well when the protein is first given. The symptoms may not, however, be manifest at the initial contact with the protein but develop at a later period, as illustrated by the following case. Egg albumen was given to an infant of three months for several days without any apparent reaction. When a coddled egg was given at the age of nine months, however, vomiting, generalized urticaria and asthma followed immediately. In other cases evidences of protein sensitization may be present during infancy and then entirely disappear, but after several years either similar or, as more often is the experience, different clinical manifestations develop. Thus a patient who has never received egg or cows' milk may have eczema throughout infancy which entirely disappears, to be followed in early childhood by asthmatic attacks with or without eczema. It is easy to understand the constant production of symptoms in a person once he has become sensitized to protein, as the avenues for entrance of protein are so very numerous and the patient is so constantly brought in contact with protein; but the manner in which the primary sensitization takes place is not so readily explained.

Sensitization may be acquired, it may be conveyed from the mother to the infant or it may be inherited. It is quite conceiv-

[5] A Case of Hypersensitiveness to Cows' Milk, Am. Jour. Dis. Children, xix, p. 46.

able that a person might become sensitized through an open wound in the skin, through the mucous membranes of the gastro-intestinal tract and various other ways. Sensitization is acquired undoubtedly in one of these ways in a certain number of cases. The transference of sensitization from an animal to the offspring, which has been demonstrated by Wells[6] and others, would suggest that human sensitization might take place in the same way. While not improbable it undoubtedly is infrequent. Experimental transference of sensitization differs greatly from human sensitization. In animals the sensitization transferred from the mother lasts but a few weeks and is not transmitted from generation to generation, while in human sensitization quite the reverse obtains. In all probability sensitization is inherited in those patients who exhibit manifestations when they are brought in contact with the protein for the first time. A family history of sensitization can be obtained in nearly all of these cases, and there are numerous cases recorded in which the sensitization has been transmitted through several generations. The sensitization, which does not have to be to the same protein, may be transmitted through the maternal or paternal ancestors. The studies of Vander Veer and Cooke substantiate this view. They showed that hypersensitiveness to protein may be inherited, and that in a general way it follows the principles of the Mendelian law of heredity.

Hypersensitiveness to protein may be established by observing the clinical symptoms which are caused by the different substances and from the history. A history of hypersensitiveness may be obtained not only from the immediate members of the family, but in the family history dating back for several generations. The occurrence of asthma, eczema, urticaria, etc., in any member of the family is suggestive evidence of hypersensitiveness. Such a history is found in a large proportion of the patients, as illustrated by the following cases: A patient, aged five years, who suffered from asthma, gave a history of asthma having occurred in the paternal great-grandfather, grandfather and the father. The skin test in this patient was positive to the protein of egg. In another patient who had asthma following the ingestion of egg the first and second cousins had an idiosyncrasy to egg.

The symptoms oftentimes are so striking and so characteristic that they afford abundant proof of hypersensitiveness. In other cases the symptoms may be so indefinite that the illness does not appear to be related to protein sensitiveness. The local reaction which is produced when protein is applied or injected into the skin of hypersensitive persons is accepted by the majority of observers as an evidence of this state. The cutaneous or intracutaneous method may be employed for this purpose.

[6] Jour. Infect. Dis., 1911, 160.

In the cutaneous method the skin is scarified with a needle or von Pirquet scarifier and the substances used for the test gently rubbed in. The scarification should be superficial and blood should not be drawn. A positive reaction is shown by the appearance of an urticarial-like wheal at the point of scarification. The reaction appears within the first five minutes, increases rapidly and reaches its height in ten to fifteen minutes. It gradually subsides, but in the majority of instances the edema persists thirty minutes or more. A control test should always be made, as in certain individuals a slight erythema with edema may appear at the point of scarification alone. A slight reaction may take place about the substances which react negatively, but it is easily differentiated from the positive reactions. It is never so intense and disappears within ten to fifteen minutes. The pure dried proteins for this test may be obtained from a number of commercial laboratories. When they are used a drop of tenth normal sodium hydrate solution is mixed with the dried proteins to facilitate solution.

In the intracutaneous method the protein in solution is injected into the skin by means of a small tuberculin syringe and fine needle. A positive result is indicated by a reaction similar to that obtained with the cutaneous method. The erythema and the edema gradually increase and attain their maximum height in the first fifteen minutes. They persist usually for thirty minutes or more. A reaction often occurs at the site of the control and of the negatively reacting substance, but it is never so intense, and the area of edema reaches its maximum diameter in five to ten minutes and gradually subsides within fifteen to twenty minutes. At times the erythema marking the site of the injection may persist in positive reactions for from twelve to twenty-four hours. It is advisable to observe the reaction for some time, for that which may at first appear to be a negative reaction occasionally becomes a positive reaction (delayed). The true reaction has to be differentiated from the traumatic or non-specific reaction which sometimes occurs, but this should not be difficult. When the reactions are negative by the cutaneous method they should be repeated with the intracutaneous method. The reactions from the intracutaneous method are more difficult to interpret than are those from the cutaneous method; on the other hand, they are more delicate. As a rule the reactions are sharp and distinct and with experience a differentiation between negative and positive reactions is not difficult.

When properly performed and interpreted, accurate information regarding the sensitiveness to the proteins tested is obtained with this test. A positive reaction indicates sensitization and a negative reaction indicates non-sensitization. Equivocal reactions may occur. A patient may exhibit clinical manifestations and give a negative reaction or a positive skin reaction may be present without the patient giving any clinical signs of sensitiveness. These are

exceptions to the rule and are seen infrequently. Care should be used in making the tests, as severe and alarming symptoms may follow the application of protein to the skin in the highly sensitized patient. One infant, hypersensitive to cows' milk, had a severe systemic reaction following the cutaneous application of a dilute solution of cows' milk, and another infant with a generalized eczema presented the symptoms of anaphylactic shock following the intracutaneous injection of a 1 to 100 dilution of egg white. Also a boy of seven years, who was hypersensitive to egg, reacted violently with urticaria, angioneurotic edema and asthma after the cutaneous application of a 1 to 100 solution of egg white. Similar reactions have been observed in other patients. The most severe reactions have followed the test with the proteins of egg white, cows' milk and of pollens. That systemic reactions may follow the inoculation of protein in the skin of a sensitized person is not surprising when one considers the infinitesimal amount of protein which will incite an attack of asthma in a person sensitive to horse dander, the pollens of grass, etc. In infants and children the reaction to only one protein should be determined at a time and the cutaneous method should be tried before the intracutaneous method.

Infants and young children, as a rule, are not sensitive to such a variety of proteins as are adults, but even in them a number of different proteins have to be used in testing for sensitization. The protein of egg, milk, cereals and meats, horse serum and dander, timothy, red-top and rag-weed are the more common substances to which children are sensitive. The selection of the proper proteins for the test, obviously, is a matter of much practical importance. Information necessitating the test with other proteins may be obtained after careful investigation. This is illustrated by the unique experience with a young girl with asthma who gave negative reactions to the proteins used in the routine tests. The asthmatic attacks occurred only when the patient was in one locality. After careful questioning it was found that the attacks were incited by handling purple asters.

As mentioned above, attention is usually attracted to this condition by the occurrence of eczema, asthma, hay fever, urticaria and angioneurotic edema or from the history of vomiting and diarrhea and general prostration when a certain food is given. The symptoms may be limited to one manifestation or various manifestations may occur in the same patient. The degree of sensitization as determined by the symptoms varies not only in different patients but in the same patient from time to time. Patients are frequently seen who come in contact with the offending protein, and yet there may be no clinical manifestations or they may be slight for long periods at a time, and then a severe reaction will occur. On the other hand, even the most minute quantity of the offending protein

is followed regularly by a violent reaction. The patient may lose his sensitiveness altogether or it may persist through life. Sometimes sensitiveness to other proteins is acquired.

All investigators have observed in these patients that there may be not only the history of sensitiveness to a number of substances but that the skin test is usually positive to more than one protein. The same patient may be sensitive to any one protein or to any combination of proteins from the same animal, or from the seed, the pollen and the leaves of a plant. On the other hand the same person may be sensitive to a number of proteins less closely related, as the protein derived from a plant and from an animal. This is true in asthma and eczema, in fact, in all of the clinical manifestations of protein sensitization. In the patient studied by Schloss, positive skin reactions were obtained to egg, oatmeal and almonds. In the patients with eczema studied by the writer,[7] positive reactions were obtained with the protein of human milk, cows' milk, barley and horse serum. A patient of seven years with eczema, urticaria and hay fever gave positive reactions to the protein of egg, barley, horse serum, walnuts and rag-weed. That these patients are sensitive to more than one protein, even closely related proteins and to proteins unrelated biologically, is not so surprising when it it is remembered that the specificity of the anaphylactic reaction in animals is determined not only by the biological origin of the proteins but by their chemical structure.

A phenomenon comparable to the refractory state or anti-anaphylactic state in animals is occasionally seen. Schloss[8] observed this in two patients who developed a generalized urticaria within one to three hours following the ingestion of egg. The positive skin reaction disappeared for twenty-two to forty days, and during this period the ingestion of egg was not followed by the usual clinical manifestations. With the reappearance of the skin reaction, egg again caused an urticaria. In one patient with asthma due to egg, whom I was desensitizing by subcutaneous injection of the protein of egg, a similar phenomenon occurred. A severe attack of asthma was precipitated by the ingestion of egg which the child obtained without the parents' knowledge. The skin reaction was positive for a period of ten days, after which the reaction was not determined, but the asthma did not recur for nearly two months; during this time she ate egg daily. It would be of much therapeutic value were it possible to produce the refractory state in a sensitized patient, but at present no satisfactory method has been devised.

Treatment of patients with hay fever and asthma due to the inhalation of pollens, the emanations from animals and absorption

[7] Blackfan, K. D.: Am. Jour. Dis. Children, xxi, 441.
[8] Tr. Am. Pediat. Soc., 1915, xxvii, 60.

from bacterial proteins has been extensively carried out by a number of workers. The procedures employed are so well known that further reference will not be made to them here. I shall, however, mention briefly the essential principles regarding the management of those patients who, on account of their hypersensitiveness to the various foods, develop eczema, urticaria, asthma, etc.

The treatment may be carried out by absolutely omitting the protein from the diet or by the process of desensitization. In certain cases a combination of these methods may be used.

Omitting certain proteins from the diet may occasion so much difficulty that it is oftentimes unsatisfactory even with the undivided attention of a responsible attendant. Also such a procedure should be undertaken with caution, especially in infants, as much harm can be done if in addition to the symptoms of hypersensitiveness there are added severe disturbances of nutrition. This is particularly liable to occur when milk is withheld from the diet of infants with eczema. In these patients, although it has been shown that the eczema can be benefited by temporarily withholding milk and other protein foods, it seems to me that treatment of their hypersensitiveness should not be started until they have reached the age when milk does not play such an important role in their nutrition.

It may be found by experience that the absolute omission of the protein is not necessary, as there is a very considerable variation in the reaction of different patients to the ingestion of various food proteins. A patient may be able to eat small quantities of a food without symptoms while large amounts bring out a severe reaction, or a patient may be able to take the food if it has been subjected to a high temperature, which renders the active properties of certain proteins inactive. The specific protein may not be present in a sufficiently high percentage in certain foods to bring about a reaction when ingested even though a positive skin test has been obtained.

Desensitization of the patient to protein is by all means the most satisfactory method of procedure. The time required for desensitization depends largely on the degree of sensitiveness and varies with each patient. The subcutaneous injection method is tedious, and, as it is particularly trying to infants and young children, I have come to rely almost entirely on desensitizing them by administering the protein by mouth. Meats, milk and cereals may be given in small amounts in solution. The protein of egg is best given in capsules.[9] The initial dose is that which fails to give a

[9] I am indebted to Mr. Dunning, of Hynson, Westcott & Dunning, of Baltimore, for his assistance in the preparation of the egg-white in capsule form, which has been used in these cases.

positive skin reaction. The rapidity with which the amount is increased depends to a great extent on the degree of sensitiveness. In each case the process of desensitization should be controlled by frequent skin tests. The aim should be not only to have the patient able to ingest the protein without a systemic reaction but to secure a negative skin reaction. It is surprising how difficult it may be to accomplish the latter. For practical purposes desensitization may be said to be completed when the patient is taking average amounts of the substance without recurrence of the symptoms. It should be remembered that the proteins, even after the patient has become able to take them by mouth in quantity, must be given regularly, as there is always the possibility of a return of the symptoms if this is not done.

Patients with only one clinical manifestation, as those who suffer from eczema, urticaria or asthma, and in whom there is a positive skin reaction to only one protein, should be given a diet from which the protein has been excluded. This should be maintained until the symptoms have disappeared. After that, desensitization may be begun by the administration of the protein to which he is sensitive.

Patients who are susceptible to a combination of proteins are the most difficult to treat. The special proteins to which they are sensitive should be excluded from the diet, and in addition protein from eggs, meat and milk even if a negative skin test is obtained to them. The reason for excluding such foods is more or less empirical. After the clinical manifestations have subsided entirely the proteins to which the patient is least sensitive, as shown by the skin test or by the reaction following their ingestion, are administered. After there has been no return of the symptoms for some time the process of desensitization with the protein which gives the most intense reaction may then be commenced. Recurrence of the symptoms at any time necessitates the withholding of the special proteins from the diet until the symptoms have subsided. Desensitization is then begun again.

Successful therapeutic results may be expected in patients who are unable to take various foods without the development of eczema, urticaria, asthma, etc., if the patients are hypersensitive to protein and if the treatment is consistently and thoroughly carried out.

THE COLON IN CONNECTION WITH CHRONIC ARTHRITIS (ARTHRITIS DEFORMANS).[1]

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In July, 1912, a single woman, aged thirty-four years, a school-teacher, was referred to me for treatment of an intestinal condition. She had a typical polyarthritis involving the phalanges, wrist, elbow, tarsal, ankle- and knee-joints, which in five years had reduced her to an invalid's chair existence. Her relapses of joint involvement were frequent, each attack rendering the joints more crippled in a permanent way. A constipation came on with the initial joints affected (both elbows), and she stated that if her bowels had not moved that day she was distinctly stiffer throughout the body that night. She had lost weight, her tissues were flabby, a psoriasis had developed, the liver was noticeably enlarged and there was a slight amount of albumin in the urine, with many granular casts. The studies of the feces showed the presence of gas-bacillus infection of the gut. She was treated by a diet high in calories, but low in calcium, and by strains of viable Bacillus coli rectally administered. The treatment was kept up for seven months, at which time she was markedly improved. In the fall of 1913 she resumed her work as teacher of French in the Wadleigh High School and has not lost a day since. She lives the life of a normal woman, attends to her apartment after school hours, cooks her own foods, goes to the theater and dances in the evenings, and, with the exception of some crippled joints, in which there has not been one remission from the beginning of treatment, she is a normal woman.

This happy result in the treatment of an intestinal toxemia seemed to qualify me in the eyes of some lay people as one especially able to treat such conditions. In the New England town that the case came from there were three others that soon were under observation, and from this nucleus it has spread from Maine to Pennsylvania until today 79 cases, supposedly like hers, have been seen. These have comprised a group of cases that deserve recording, both as to the findings and results accomplished. Of these, 31 were deemed unsuitable to be classed as typical ones of polyarthritis. They were made up of instances of gouty joints, syphilis, myositis, true articular rheumatism more or less resolved, acute joint involvement from manifest focal infections that were easily removed (nothing more being done in the treatment of the arthritis), and 3 extreme cripples so seriously involved with manifest disease of internal organs (mainly

[1] Read before the Academy of Medicine, March 19, 1920.

liver, kidneys and heart) that they were judged unfit for both study and treatment. The 45 remaining ones I desire to present.

Of these the average duration of joint involvement was three and seven months. The knee-joints, left, right or both, were initial in 12 cases, the ankles in 7, the elbows in 11 and other joints in the 7 remaining. Manifest focal infections were present in the tonsils in 13; in dead tooth pulps, apex abscesses and pyorrhea, in 10; urinary tract, 3; appendix, 3; gall-bladder, 2; prostate gland, 2; female pelvis, 1; head sinus, 1. This makes 35 of 45 having manifest infection. An infectious disease of years before, healed or dormant tuberculosis, cystitis without involvement of the pelvis of the kidney or substance, boils, etc., were thrown out of etiologic consideration; 14 were men and 31 were women. The average age of the 45 cases was thirty-one years when seen by me.

The 13 tonsil cases were properly operated upon, 1 requiring a second operation for a tab of tonsil tissue that was left behind the left anterior pillar. Improvement in the joints was quickly noticeable in 4, believed to have come about by the patient in 3 more and none being noticeable in 8. The one that showed the most marked benefit in the joints got the worst relapse. She had this six months after operation and then came under observation and study. The second best case had a relapse in the fifth week after enucleation. They were all advised to remain away for three months after operation unless the joints became noticeably more involved. In the course of seven months they all had come back with added frank joint involvements.

In the 10 oral sepsis cases the best possible attention was given. Extraction of teeth was the rule, this being done uniformly throughout the group. The devitalized teeth with apex abscesses were opened through the apex ostium and drained for three weeks. Each tooth canal was filled with gutta-percha through the apex opening; until that was accomplished it was not considered sterile. With the amputation of root ends and surgical attention to pyorrhea, as well as insistence on mouth hygiene as a daily practice, the cases were handled according to the best of modern dental attention. In some of the cases (six in number) the work extended over months of time. Thus definite time allowance for return of joint relapses was not practical. One of the cases, one of general pyorrhea with apex abscesses and extraction of all of the teeth, claimed marked benefit in the joint symptoms with but one slight relapse in three years. The patient feels the benefit satisfactory enough not to warrant a long trip to New York City for further study and observation. The other 9 cases came under observation even after all of this work, expense, pain and trouble. On the occasion of relapse, or there being no benefit in the joint symptoms, films were again taken of the teeth so that this source of infection could definitely be thrown out of consideration. In the six that had relapses the average

length of time of this after the dental work was concluded was seven months. The other three had no joint benefit whatever.

The 3 appendix cases were operated upon, 1 claiming a moderate benefit, but relapses establishing themselves in the second month afterward. The 2 gall-bladder cases (both cholelithiasis with chronic cholecystitis), in which cholecystectomy was done, were not improved, one apparently being made worse by operation for unknown reasons. The 3 renal cases are difficult to conclude on. One was a woman with a badly diseased but 50 per cent. functioning left kidney. A Gram-positive bacteria was always present in the urine from that side. This organism was not identifiable but easily grown on blood agar, and a vaccine was made and administered subcutaneously. This was kept up for five months together with regular washing of the pelvis of the kidney on that side. A nephrectomy was then done, although the woman seemed to have been benefited in the joint symptoms. A generally diseased and vacuolated tuberculous kidney was removed. The urine cleared of pus and the vaccine organisms. On the tenth week after the operation, when distinct benefit was apparently coming about, a relapse in the joint symptoms occurred, rendering the patient unable to leave the bed for nearly three months. She was then moved to the city for further observation. The other 2 cases were those of Bacillus coli pyelitis that cleared on vaccine, hexamethylenamin, renal pelvis irrigations and length of time. No benefit occurred in either one in the joint condition even after the urine had been clear for three months. The prostate cases were enlarged prostates. Both were considered chronic disease of the seminal vesicles originally from Neisserian infection. Both were treated by massage, irrigations of and installations into the posterior urthera. One developed a prostate abscess when under treatment, was operated on and made a clear local recovery. Neither was benefited in the joint symptoms. A case of double pyosalpinx had both tubes removed with benefit only to the pelvic distress, and one of double ethmoidal disease with an infected superior maxillary sinus was thoroughly operated upon, drained and irrigated, also without other than benefit to local symptoms.

Here then were 35 cases of typical polyarthritis of the chronic type with focal infection, all of which were carefully and thoroughly treated in ways that are known to be the best, and yet all but one has received no benefit in the joint conditions. The 34 cases were finally placed under observation for metabolic and gastro-intestinal study, which with the 10 that showed no manifest focal infections made up 44 cases. Each was placed upon the following test diet, which was graded in instances of lighter weight than 140 pounds, according to what that would be:

"The diet mentioned is to be adhered to strictly for three full days, namely, seventy-two hours. The stools and urine of the first

forty-eight hours after its institution are of no value for examination. If constipation exists the bowels are to be moved by injection. After the forty-eighth hour from the beginning, providing the bowels have moved during that time, the entire next stool is to be saved and examined. No purges are to be taken, but a glycerin suppository or an enema may be employed to obtain the stool required. A covered small tin can or a glass jar can be used as a container. A twenty-four-hour collection of urine should accompany the stool, this being started at the end of the forty-eighth hour after the institution of the diet. Start with an empty bladder and void for the last portion at the twenty-fourth hour. Take no medication by mouth during the three days and continue your activities as you have been doing.

Morning: Two thin slices of well-baked bread, with butter liberally applied; one pint of oatmeal gruel, made of about 40 grams or $1\frac{1}{2}$ ounce of oatmeal; 10 grams or $\frac{1}{3}$ ounce of butter; 200 grams or $6\frac{2}{3}$ ounces of milk; 300 grams or 10 ounces of water (all strained). One egg cooked in any form.

11 A.M.: Milk, one-half pint or one glassful.

Noon: A good-sized piece of steak or roast beef, chopped or cut into very fine pieces, about 200 grams or 4 ounces, and served on a slice of toast; one bowl, about 250 grams or $8\frac{1}{3}$ ounces, of mashed potato, with 20 grams or $\frac{2}{3}$ ounce of butter.

4 P.M.: Milk, one-half pint or one glassful.

Night: Same diet as breakfast.

Water may be taken as desired.

Attention must be paid that this diet is followed precisely. The reason for this is that careful and extensive quantitative examinations are made of the specimens sent, and unless the rules are followed accurately the laboratory findings may be misleading."

During the last twenty-four hours (from the forty-eighth to the seventy-second hour) 40 c.c. of blood was extracted, ten being employed for the Wassermann test, the remaining 30 c.c. being placed in a bottle containing a few drops of 20 per cent. potassium oxalate solution. The blood was taken at about the forty-eighth hour from the onset of the diet before breakfast.

The Wassermann test was negative in all of the instances. This is not surprising, because of all of the cases in which a positive Wassermann was present, mercurial injections were carried out as a routine. Nine of the focal infection cases had a positive Wassermann, all receiving mercurial injections during the time they were under observation by others, and those that gave a definitely positive Wassermann at the initial examination were judged syphilitic and are not included in the 45 cases reported. Still it was considered wise to do another Wassermann before the beginning of the metabolic and gastro-intestinal studies. A case might have been missed in the first instance and be caught here, or a case might have begot a syphilis in the length of time of their operative

procedures. It was also deemed wise not to employ the ingestion of glucose before the blood was drawn. The reason of this is that because many instances of chronic intestinal toxemia show a sugar intolerance to this method. The sugar intolerance after ingestion of glucose is a finding in at least 20 per cent. of the saccharobutyric toxemias. Thus it was thought best to estimate the sugar content under normal conditions.

None of the 31 cases showed a hyperglycemia, taking 0.1 per cent. as the standard. In one of them a colorimetric reading of 35 (0.13 per cent.) was obtained, but subsequent examination did not sustain it.

The creatinin estimations averaged in 43 instances 2.2401 mgm. Taking 2.2375 mgm. as a standard, 13 of 31 cases were somewhat elevated. There were others, however, that were distinctly below this figure. Because in saccharobutyric toxemias about one-half of the cases show a slightly elevated creatinin content in the blood, these findings were taken as non-significant in so far as chronic arthritis was concerned.

The uric acid estimation in 29 cases gave an average of approximately 250 mgm. per 100 c.c. of blood. The same negative findings may be said of the non-protein nitrogen estimations, the average in 31 cases being 7.7. mgm. in 100 c.c. of blood. Cholesterol total solids and chlorides were not estimated. Several of the cases in which markedly reduced states of body existed showed slight degrees of acidosis. These findings were considered as a secondary condition and etiologically or symptomatically non-important. Many had degrees of simple anemia, sometimes with a lowering of the erythrocyte count.

In all of the cases routine examinations of the urine were made. Attention was paid to the indican and uroresine presence, and sulphate partitions were made in all of them. The presence of an excess of the conjugate sulphate, oxalic and uric acids and a chloride and total solid decrease were considered significant. Forty-four urines with abnormal findings were found.

The stools were carefully examined; notes were made of reactions; study of food detritus; search for ova (none found); estimation of mucous content; Gram-differential studies and relative countings; the fermentation tests and studies of gas contents and character; studies of sedimentary bacterial growths grown anaërobically and aërobically, with animal inoculation, were done. Taking normal standards there were forty-four departures from it. Thus with the urine and stool findings there were 44 instances of chronic intestinal toxemias: 34 were saccharobutyric in type, 2 were indolic and 8 were of mixed form.

From this practically complete significance of the colon as a cause of arthritic symptoms the cases were treated by diet, suitable to the type of toxemia and vaccines, all of the cases being kept under

treatment at least five months and diet alone advised for a year afterward. The plan of vaccine treatments and the diets employed were according to the author's methods,[2] in which the biochemical alteration method was not found necessary in any of them.

BACTERIAL TREATMENTS IN PRIMARY TOXEMIAS (RECTAL AND SUBCUTANEOUS METHODS AND VACCINE IMMUNITY).

Saccharobutyric	B. aërogenes capsulatus (rectal). Gram-positive diplococci (skin, rarely; rectal, rarely). Gram-positive single cocci (rectal). B. bifidus (rectal rarely). B. putrificus (rectal rarely).
Indolic	B. coli communis (rectal, skin). B. mesentericus (rectal). B. liquefacius (rectal). B. proteus. Gram-negative streptococci (skin). Staphylococci (skin).
Mixed	Combination of above according to predomination of fermentation or putrefaction and types of organism. The rectal method is used here altogether, and effort is made to get reactions and a leukocytosis of from 10,000 to 20,000 within eight hours after the injections.

BACTERIAL TREATMENTS IN PRIMARY TOXEMIAS (RECTAL AND SUBCUTANEOUS METHODS AND BACTERIAL ANTAGONISMS).

Saccharobutyric (heavy protein diet)	B. aërogenes capsulatus Gram-positive diplococci Gram-positive single cocci B. bifidus	B. coli (many different strains and perhaps collected from different sources); for the first two *a* and for the second two the *b* strains are best.
Indolic (low protein and high carbohydrate and hydrocarbon diet)	B. coli B. mesentericus Gram-negative streptococci Gram-negative staphylococci B. proteus vulgaris (B. Welch) B. cloaca (B. coli, polyvalent strains) B. pyocyaneus (B. coli, *a* strains) B. putrificus (B. coli, *b* strains)	B. acidophilus B. bulgaricus. B. lactic aërogenes.
Mixed (least possible amounts of food, no cheese; peeling of fruits; mostly boiled foods)	No action on antagonisms possible by rectal or subcutaneous methods excepting when a predominant type of bacteria is present.	

The difference between the *a* and *b* strains of Bacillus coli is that it does not produce gas in saccharose; the *b* does. The effects are the same on all the other sugars and on the coagulation of milk.

[2] Therap. Gaz., February 15, 1920.

Occasional recourse in the debilitated cases to the low calcium diet as advised by Bovaird was employed. This, however, was not considered specific in any sense, but is useful in building up general tone and vital strength. Anticonstipation additions of bran preparations, prunes cooked in lactose sugar, fruits twice a day, water in abundance, agar-agar, etc., were often required. A weekly dose of castor oil was advised. No physical measures of treatment were allowed until the relapses had ceased and the case had made marked improvement. Experience proved that while an occasional case is benefited by physical treatments the majority are not when relapses were running or liable to occur. The best time to begin physical treatments is from six months to one year after the last relapse, the later the better the results from them.

Cure cannot be figured in this disorder. One cannot by any treatment restore diseased tissue. Joints which have atrophy of cartilage, absorption of bone, hyperosseous growths, ankylosis, etc., never could return to normal even were one to employ a specific treatment on the cause. The mischief is done when the deformity is present. Benefit could be judged by stopping of the relapses, reduction of swelling and pain of the joints and general improvement of the body and increase in usefulness of the joints. In addition, all of these would have to be viewed with a conservative attitude. In a group of cases one sees not uncommonly some that for some unknown reason have run a short course of slight involvements and then no more progression. The next case in the same several months of time might be bedridden with ebonization of all of the joints. In groups the cases run very irregularly. With the majority, however, the tendency is downward by relapse, the already affected joints becoming worse and the non-involved joints becoming affected. The only standard to figure benefit on is a relative one based on how the patient was before treatment and how afterward in sustained ways. The cessation of relapses is an important factor in this, in my opinion the most important one. Reduction of swellings of the joints is accomplished only in the periarticular tissues, and it is by these two that increased usefulness of joints is accomplished. What, perhaps, is the next important factor in some of the cases is an improvement in general body, such as in the loss of weight, condition of body tone, the anemia, a secondary renal disturbance that may and often does approximate a true nephritis and status of tone and function of the liver and heart. Thus in any case we can only record improvements and perhaps classify them as none, moderate or marked.

In 44 cases treated by the measures mentioned, marked improvement was observed in 21, moderate in 19 and none at all in 4. Those that had physical measures of treatment, late after the diet and vaccine treatments, made more marked benefit in all but 9, this including the 4 mentioned above.

Conclusion. Focal infections are commonly met with in cases of arthritis deformans, which, when corrected surgically, do not actually benefit the chronic cases, although it may be striking in results in arthritis of only a few weeks' or months' standing.

The tonsils are the most often affected, the teeth next and other sites less frequently. The colon, however, was the commonest source of infection of them all, the organisms met with in order of frequency being the Bacillus aërogenes capsulatus, diplo- and single Gram-positive cocci, Bacillus putrificus, pathogenic types of Bacillus coli communis, staphylococci and streptococci.

On the basis of what can be estimated by blood chemistry today there is no reason to believe that arthritis deformans is due to constitutional errors, a view commonly held, particularly by the older clinicians. It is far more logical to believe that the condition in each instance is due to focal infection somewhere in the body, the intestinal canal being the most frequent site.

Whatever manifest focal infection is found should be treated surgically, and when no benefit is noted, complete examination of stools and urine are in order because treatment directed here is well worth the trouble in the results probable of being accomplished.

Dieting according to the type of bacterial infection (toxemia) present in the gut and bacterial treatment commonly offers distinct benefit in the cases.

Constipation and debility should be corrected by diet and not by drugs.

There is no possibility of cure in the true sense, only benefit can be accomplished, and when this is sustained over lengths of time it represents the best that can be accomplished. Joints crippled by changes in the anatomy remain that way permanently.

There is good reason to believe that in the early course of this disorder if attention is given to the colon as well as to the other focal infections many would be saved a fate of chronic joint deformity and invalidism.

IMPROVEMENT IN GRAVES'S DISEASE SUBSEQUENT TO SEVERE FOCAL INFECTION.[1]

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We have recently had occasion to study two patients with Graves's disease, both of whom manifested very great improvement subsequent to severe acute infection.

[1] I wish to express my thanks to Dr. Newburgh for the privilege of reporting these cases.

As is well known, many writers have repeatedly pointed out that infections of any sort may have a markedly deleterious effect upon the thyroid, and, indeed, infection has been given an important role in the etiology of Graves's disease.

Vincent,[2] for example, has reported that of 156 cases of acute rheumatic fever which came under his observation, 86, or 68.3 per cent., showed painful tumefaction of the thyroid gland which disappeared with the symptoms of rheumatism.

Billings[3] likewise has observed many instances of thyroid enlargement, usually of the chronic type, in which various focal infections were associated with evidence of thyroid intoxication.

Jennings[4] has reported two cases of measles occurring in patients with preëxisting Graves's disease. In one patient, in whom hyperthyroidism was marked, death resulted during the course of the measles. In the other hyperthyroid symptoms were mild, but the attack of measles so aggravated the condition of the thyroid gland that four weeks later surgical intervention was deemed necessary.

In those cases of Graves's disease which have come under our observation the appearance of an acute infection very commonly has led during the course of the infection to an exacerbation of all symptoms of thyroid disease. Accordingly the search for and elimination of focal infection has become an accepted routine in the medical treatment of this condition, and the improvement seen following the removal of such foci has frequently been striking.

With these facts in mind the occurrence of improvement as a result of infection seems at first thought to be paradoxical. However, as Beck[5] pointed out, one would expect the first effect of infection to be irritative, and hence productive of thyroid hyperfunction, and that later effects of the same infection may be degenerative changes leading to hypofunction. Indeed, Vincent[6] mentions one case in his series which would definitely fall in this category. Thyroid hypertrophy which had appeared in association with rheumatic fever gradually receded, so that at the end the gland was left sclerosed and atrophic. Several instances are cited by Beck[7] in which well-marked symptoms of thyroid insufficiency appeared following protracted acute infections. Hertoghe[8] feels that all infectious diseases of childhood and of later life fall heavily on the vitality of the thyroid gland. Similarly, Ord[9] states that often the

[2] Sur la Réaction Thyroïdienne dans le Rhumatisme Aigu et sur l'Origine Rhumatismale de certains Cas de Goitre Exophthalmique, Compt. rend. Soc. de Biol., 1907, lxiii, 389.

[3] Focal Infection, The Lane Medical Lectures, 1917, Appleton & Co., p. 103.

[4] Two Cases Showing the Effect of the Incidence of English Measles upon Preexisting Graves's Disease, Lancet, 1918, i, 906.

[5] The Relation of Chronic Infection to Thyroid Deficiency, Southern Med. Jour., 1918, xi, 492.

[6] Loc. cit.

[7] Loc. cit.

[8] Thyroid Deficiency, Med. Rec., 1914, lxxxvi, 489.

[9] Myxedema, Tr. Clin. Soc., 1888, xxi, 298.

atrophy which results in myxedema is due to inflammatory destruction of the glandular tissue. Cases have been reported by Albo[10] and others in which influenza apparently precipitated symptoms of thyroid deficiency.

Whether or not the thyroid itself is actually invaded during infection can only be conjectured. That such invasion does take place is certainly not unlikely. McCallum[11] has suggested that infection reaches the thyroid from the pharynx and sets up in the gland a non-suppurative thyroiditis which destroys many of the cells and leaves scars through the gland, after which hypertrophy of the remaining tissue occurs. Gilbride[12] studied bacteriologically 14 operated cases of goiter, 6 of which were exophthalmic and 8 cystic in type. He succeeded in isolating Micrococcus tetragenous from one gland from the exophthalmic group, and from one gland from the cystic group he isolated Streptococcus vermiformis of Sternberg. Such study fails, however, to accurately represent the possible frequency of thyroid invasion. Operations are avoided during acute infection, and obviously it is during the period of active infection that we would expect the highest percentage of positive tissue cultures. It would be unwise to attach too much significance to the finding of Streptococcus vermiformis in the culture from one cystic gland, for the frequency with which this organism occurs as a contamination in tissue culture is well known.

We wish to present two cases of hyperthyroidism, both of which showed striking improvement following severe infection.

Case I.—Mrs. C., aged forty-eight years, housewife, married, entered the hospital March 10, 1917, complaining of tumor in the thyroid region, palpitation of the heart and pain over the region of the ensiform. The family history was negative. She had never been pregnant, and until two years ago her menstruation was normal. At this time the flow became profuse and currettage was done. Save scarlet fever at twenty-two the past history was unimportant.

In the summer of 1916 she became very nervous and noticed a marked tremor of the hands which, during August, was so pronounced that she could scarcely handle dishes. She began to have drenching night-sweats, which persisted through the fall of 1916. On October 14 she became prostrated and would have fallen if someone had not supported her. She first noticed at this time a small enlargement in the thyroid region which had progressively increased in size until the time of her admission. She went to bed October 14 and remained there six weeks. For several weeks after getting up

[10] Postinfluenzal Thyroid Insufficiency, Progresos de la Clinica, 1919, vii, 122; Abst., Jour. Am. Med. Assn., lxxxiii, 157.

[11] The Pathology of Exophthalmic Goiter, Jour. Am. Med. Assn., 1907, xlix, 1158.

[12] Culture from the Thyroid Gland in Goiter, a Bacteriological Study, Jour. Am. Med. Assn., 1911, lvii, 1988.

she had attacks of pain under the sternum so severe that at times it was necessary to lie down. Tiredness, trembling and dyspnea

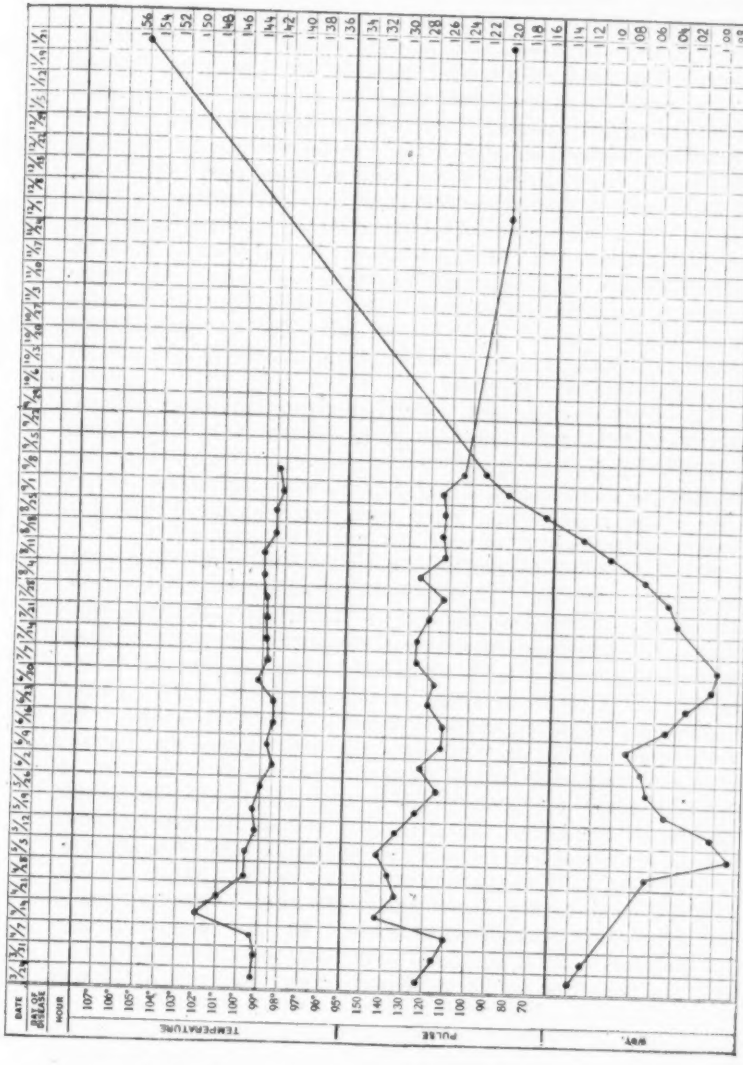

CHART I.—Case I. Chart showing temperature, pulse and weight by weeks. Average temperature and pulse readings for the period indicated are recorded.

were marked. There was no diarrhea and her appetite was quite variable. She had lost fifty pounds in the past year.

Examination March 13, 1917, showed a poorly nourished woman weighing 115 pounds. The skin was rather deeply pigmented throughout. Pupils were round, equal, rather widely dilated, but reacted normally. The palpebral fissures were widened and there was considerable lagophthalmos, together with failure of convergence. The forehead wrinkled normally on looking up. Scleræ and conjunctivæ were normal. The tongue protruded in the midline with marked tremor. Tonsils were slightly enlarged. There was slight bilateral enlargement of the thyroid gland. No thrill was noted, but a distinct bruit could be heard over both lobes. There was marked pulsation of the great vessels of the neck. Examination of the lungs revealed no abnormalities. The apex impulse of the heart was best felt in the fifth intercostal space in the midclavicular line. There was no enlargement to the right. The heart-rate was rapid and the sounds clear and forceful. No murmurs were heard. A-2 was greater than P-2. The abdomen showed nothing unusual. Except for a fine tremor on extending the fingers the extremities were negative.

The urine was negative. Blood-pressure, 155 to 85. Blood: red blood cells, 4,250,000; hemoglobin, 80 per cent.; white blood cells, 6800; differential count: neutrophile polynuclears, 69 per cent.; eosinophile polynuclears, 2 per cent.; small lymphocytes, 18 per cent.; large lymphocytes, 5 per cent.; transitionals, 3 per cent.; large mononuclears, 3 per cent.

She was placed in isolation, strictly confined to bed and given forced diet. By March 28 there had been no increase in her weight. On April 7 she complained of chilly sensations and her temperature was 101°. A few spots were seen in the posttonsilar region. There was some difficulty in swallowing solid food and she was placed on a liquid diet. Her white count at this time was 11,150. Throat culture was reported negative for Klebs-Loeffler bacillus. She grew rapidly worse, the tremor became very marked and she was excessively emotional there being some delusions. On April 15 respiration was of Cheyne-Stokes type, and there was considerable acetone in the urine. She was given sodium bicarbonate intravenously, and one hour following she had a chill lasting ten minutes. Throughout April 16 she was stuporous, but was easily aroused. She was slightly disoriented and there were involuntary bowel movements and incontinence of urine. The pulse was quite irregular, and she continued irrational on the 17th and 18th. By April 21 the tonsillitis had subsided. Blood culture taken April 13 was reported sterile on the 25th.

On April 28 the goiter had become smaller in size and had lost its hard feeling. Exophthalmos was somewhat less and lagophthalmos was absent. Nervousness was much diminished and she herself was conscious of improvement. During the week ending May 21 she gained five pounds, palpitation was less marked and the thyroid

gland was no longer palpable. She improved steadily until June 21, from which time her appetite became poorer and her weight, which had reached 108 pounds, had fallen by July 7 to 100 pounds, and she was quite depressed because of the apparent lack of progress. In the following week she began to improve again. July 14 she weighed 102 pounds; July 21 her weight was 104 pounds and on the 24th she was allowed to be up in a chair for the first time. She continued to gain weight, weighing 105½ pounds July 28, 107¾ August 4, 110 August 11, 113 August 18, 117½ August 26 and 120 September 1. At this time she felt fine and walked about the ward considerably. There had been but little diminution in the pulse-rate, but she no longer was conscious of palpitation. September 28 she weighed 122½ pounds and was discharged, feeling quite well. December 2, 1917, a letter from her stated that she was feeling perfectly well and her pulse averaged 85. On January 24, 1918, she returned for reëxamination. She said that since leaving the hospital she had felt fine and she herself was convinced that no signs of the disease remained. Her weight was 156 pounds and examination showed her neck and eyes to be perfectly normal.

Case II.—C. O., aged twenty-three years, male, machinist, unmarried, entered the hospital October 9, 1919, complaining of nervousness, weakness, tachycardia, exophthalmos and tumor of the neck.

The family history was negative. At the age of thirteen he had a perforating injury of the right eye. From the age of ten to sixteen there was almost a constant succession of boils, which he stated were cured by vaccine.

In April, 1918, he had a severe sore-throat, lasting two weeks, which was accompanied by iregular chills and fever, but without joint symptoms. On May 6, while operating an electrical machine he received a severe shock, which threw him to the floor and caused him to lose consciousness for a period of five minutes. After a short rest he was able, however, to go on with his work. That night at the supper table he noticed a tremor of the hands so marked that he was unable to hold a glass of water steadily. For the next two weeks he continued to work, but there was a gradual increase of weakness and loss of strength, so that at the end of that time he was hardly able to climb a flight of stairs, and he had lost fifteen pounds in weight. Early in June he was called by his local draft board and rejected for army service because of "leakage of the heart." This worried him considerably, and upon the advice of his physician he remained in bed for a period of three months, but made little improvement. His weakness and nervousness increased, his eyes became more prominent and he steadily lost weight in spite of an exceptional appetite. He entered the hospital October 9, 1919.

Examination showed a fairly well-nourished young man weighing 115½ pounds. There was marked exophthalmos, definite lagoph-

thalmos and failure of convergence. The right pupil was pyriform in outline, but both reacted to light and accommodation. Tonsils were moderately enlarged and the postcervical glands were palpable. There was a uniform soft enlargement of both lobes of the thyroid, and over both lobes a thrill was felt and a two-way bruit heard on auscultation.

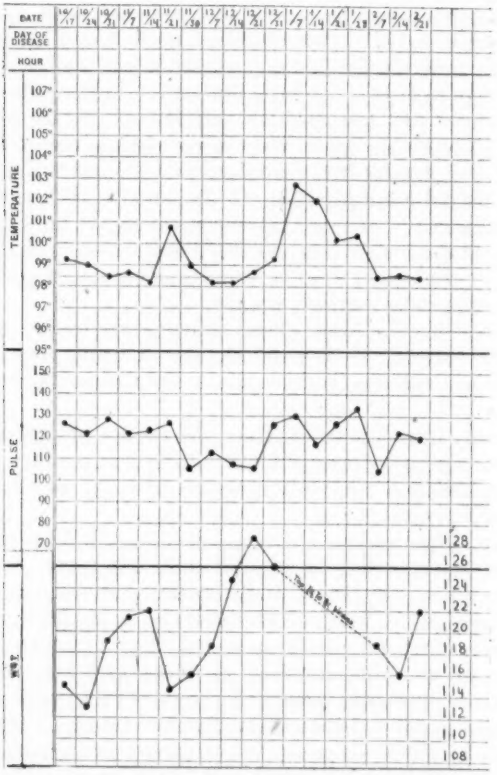

CHART II.—Case II. Chart showing temprature, pulse and weight by weeks. Average temperature and pulse readings for the period indicated are recorded.

The heart apex was in the fifth intercostal space inside the nipple line. The rate was rapid and regular, and a soft systolic murmur was heard best at the apex and was audible over the entire precordium, but was not transmitted to the axilla. A-2 and P-2 were about equal.

Chest and abdominal examinations were negative, and except for the typical fine tremor on extension of the fingers the extremities showed nothing of note. Blood-pressure 125 to 80; red blood cells,

4,080,000; hemoglobin, 75 per cent.; white blood cells, 9500. Differential: neutrophile polynuclears, 56 per cent.; eosinophile polynuclears, 1 per cent.; large lymphocytes, 36 per cent.; small lymphocytes, 7 per cent. Urine negative. Blood Wassermann negative. An orthodiagram at this time showed the round heart of chronic myocarditis with an area of 130 per cent.

Rest in bed and forced diet were ordered. After an initial loss of two pounds his weight remained practically stationary until October 26. In this period he had occasional attacks of epistaxis. He gradually gained weight from this time until November 9, when he weighed 123 pounds. Because of hypertrophied tonsils tonsillectomy was done November 11, following which a septic temperature developed. Upon examination an abscess was found just in front of the posterior pillar of the fauces, and this was lanced. After several days of hot saline irrigations the temperature fell to normal. A roentgen ray of the teeth showed an apical abscess of the left lower first molar, and on November 26 this tooth was extracted, following which his temperature again rose to 104.4°. On November 28 the thrill and bruit over the gland had both markedly increased in intensity and his weight was 115 pounds. At this time he also complained of pain in his right ear. On the 28th and 29th he had several attacks of epistaxis. In spite of these difficulties he gained a little, and on December 10 he weighed 122½ pounds. He continued to gain until December 24, when his weight was 129½ pounds. On January 2 he developed an acute rhinitis, accompanied by severe headache, earache and sweating. Mastoid tenderness appeared on the right side, and on January 5 a paracentesis was done. The ear drained freely and was subsequently treated with hot saline irrigations. On January 15 he had shown marked improvement, but the temperature still showed some fluctuations, the maximum being 100.8°. The signs of hyperthyroidism were markedly diminished: exophthalmos had decreased slightly the tremor of the hands was by no means so marked as previously and the thyroid enlargement had practically disappeared. There was marked pulsation of the great vessels of the neck, but no thrill could be felt, and there was no bruit. He continued to improve until January 22, when he contracted influenza. His temperature rose to 102° and he conplained of some stiffness of the right side of his neck. By January 28 his temperature had again returned to normal, and it remained so up to the time of his discharge. On February 5 exophthalmos was noted as being somewhat lessened, but lagophthalmos was still slightly evident. On February 10 lagophthalmos had practically disappeared. He was discharged February 21, there being at this time no neck signs save a very slight enlargement. He himself felt that the improvement in his condition was most striking. Following discharge he continued to improve, and on April 1 his weight was 185 pounds and he was feeling fine.

The course of these two cases makes it seem not unlikely that we have in them examples of infection, which either by direct invasion of the gland or by toxic action so affected the secretory tissue of the thyroid that subsequently the Graves's disease was very much improved. Whether this improvement can be regarded as the result of glandular exhaustion or actual loss of secretory tissue through damage is difficult to say. It would seem most probable that the latter explanation is the true one.

Summary. 1. As is well known, acute infections occurring during the course of Graves's disease usually cause a marked increase in the severity of all symptoms.

2. Sometimes, however, such infections apparently do injure the gland sufficiently to result in eventual alleviation of the condition.

3. Two cases of hyperthyroidism are cited in which complicating infections first caused a marked increase in the severity of the thyroid symptoms later followed, after the acute infection had subsided, by striking improvement if not cure. It is not improbable that the improvement seen is due to actual loss of secretory tissue through postinfectious sclerosis of the gland.

GLUCOSE TOLERANCE TEST IN CHRONIC VASCULAR HYPERTENSION.[1]

By James P. O'Hare, M.D.,

BOSTON, MASS.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston Mass.)

I wish to present briefly in this paper the results of 25 glucose tolerance tests done on 23 cases of chronic vascular hypertension. Hopkins,[2] Hamman and Hirshman,[3] Janney and Isaacson[4] and others have shown clearly enough that patients with diabetes, nephritis and certain endocrine disturbances cannot handle glucose taken by mouth as well as normal persons. Patients with chronic vascular hypertension can hardly be regarded as diabetics or nephritics, and as yet no endocrine disturbance has been proved in them. They, too, may show a disturbance in handling glucose. This type of case is, of course, very similar to the nephritic with hypertension. The element of retention of glucose, however, which complicates the interpretation of the glucose tolerance test in the true nephritic, apparently does not occur in the true chronic vascular hypertension

[1] Read at the meeting of the New York Academy of Medicine, April 1, 1920.
[2] Am. Jour. Med. Sc., 1915, cxlix, 254.
[3] Arch. Int. Med., 1917, xx, 761.
[4] Jour. Am. Med. Assn., 1918, lxx, 1131.

MED. NO.	11803	12459	10349	11704	9799	7761	10661	13568	12859	12940	7668	11581	11704	8743	11529	12581	11735	8920	11143	9846	11390	9799	8976	13915	12725
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GLYCOSURIA AT OTHER TIMES	○	○	+	+	+	○	○	○	○	○	○	○	+	0.2 ++	○	○	○	+	+	+ 1.5	+	+	+	4.0	2.0 +++
PHTHALEIN	65	55	55	54	62	89	64	50	55	69	76	50	54	70	72	40	52	68	50	55	56	62	44	55	65
B. U. N.	12	16	12	13	11	12	13	6	16	15	10	16	13	13	14	—	11	12	19	12	14	11	18	11	13
B. P.	185 100	186 100	240 135	190 120	190 80	160 120	188 112	250 150	186 100	224 100	260 112	260 120	190 80	278 140	194 100	225 140	260 130	216 124	190 115	264 150	230 130	190 80	214 128	175 105	208 108
ARTERIOSCLEROSIS	○	+	+	○	+	+	○	+	+	○	+	○	+	○	+	+	+	+	+	+	+	+	+	+	+

case. Undoubtedly the fundamental factors underlying the lack of tolerance for glucose in these conditions is the same. What these factors are we do not know. The 25 tests arranged as I have arranged them in the accompanying chart throw an interesting light on the subject of potential diabetes.

While following a large group of these chronic vascular hypertensive cases we noted that from time to time some of them showed a trace of sugar in the urine, occasionally enough to quantitate. Our curiosity was aroused to explain it. Were we dealing with cases of renal diabetes? While the evidence we have at hand is not sufficient to absolutely exclude this condition, it is practically certain that renal diabetes can play only an occasional part. Were we then dealing with mild diabetes? The occurrence of the sugar was so intermittent that it was obviously not practical to establish the degree of tolerance by any dietary test such as one would use in the diabetic. The glucose tolerance test of Janney and Isaacson was therefore used to see whether or not there was any disturbance of carbohydrate metabolism. This test, in its simplest form, consists in the determination of the fasting blood-sugar in the venous blood and the blood-sugar two hours after the ingestion of 1.5 grams of glucose per kilogram of body weight; 2.5 c.c. of water are used for each gram of glucose. In addition we determined the quantity of sugar present in a specimen of urine three hours after the glucose was taken and in the twenty-four-hour specimen. (The figures in the chart for the glycosuria during the test are for the three-hour period.)

In the chart on page 368 the dot represents the fasting blood-sugar, the circle and the blood-sugar two hours after the ingestion of the glucose. The normal difference should be 0.02 per cent. or less. Our cases are arranged according to the size of this difference, beginning at the left, where there is no difference, and moving gradually to the right, where the last case shows a difference of 0.22 per cent., eleven times the normal. A glance at this widening band of difference will show how these cases tend to merge into the typical diabetic reaction in this test.

In the line below the occurrence of glycosuria during the test is noted. A plus sign represents a trace. Two or more plus signs an amount sufficient to quantitate by the fermentation method, in the last two cases 4 per cent. and 2 per cent. respectively. Eight cases showed glycosuria during the test.

In the next lower line is noted those cases which showed glycosuria at times other than during the test—in all, 11 cases.

In the next lower lines are given the phthalein excretion and the blood-urea nitrogen, which, together with the two-hour renal test, which was done on each case, show normal renal function for all of these patients.

The systolic and diastolic pressures are shown in the line below and at the bottom the presence or absence of arteriosclerosis as demonstrable in the peripheral and retinal vessels. It may not be amiss to say at this point that the mere fact that no sclerosis of the peripheral vessels is observable does not exclude arteriosclerosis. The smaller arteries, which are perhaps more important than these larger ones, often show definite arteriosclerosis. The retinal vessels are the only small vessels that can be observed. These vessels are of particular importance in this disease, in that they offer us the only possible index of the small vessels of the various organs, especially of the brain.

In analyzing the results of the test we can see that the first 7 cases were not abnormal in regard to glucose metabolism, except that one showed a glycosuria during the test, No. 12568 showing 0.63 per cent. The remaining 11 cases, however, show well-marked variations from the normal, as indicated by the high blood-sugars after taking the glucose and by the very definite glycosuria in 5 cases. Surely one will admit that the last 2 cases—the first with a difference of 0.14 per cent. and a glycosuria of 4 per cent. and the last with a difference of 0.22 per cent. and a glycosuria of 2 per cent. —approach the typical diabetic reaction, if they are not actually diabetic.

There is no relation of importance between the height of the blood-pressure and the reaction in these cases. The differences in the glucose reaction could not be linked up in any way with differences in the amount of arteriosclerosis, although this may be a factor. I know of no method of measuring accurately comparative variations in the degree of sclerosis.

Two cases (9799 and 11,704) have had the test repeated. The results are of great interest in showing the variability of this glucose function. No. 11,704 showed an essentially normal reaction followed nine days later by a slightly abnormal one. No. 9799 showed (at the right of the chart) a markedly abnormal reaction. Several months later, however, her reaction was normal except for the occurrence of sugar in the urine during the test.

We know that these cases of chronic vascular hypertension are potential nephritics. Perhaps most of our chronic nephritics with hypertension develop from the purely vascular hypertensive case rather than from an acute and subacute nephritis. Are these cases potential diabetics too? My chart indicates that they are. The test of time alone will show whether they develop into true diabetics. Some of them will undoubtedly die from other causes before diabetes is definitely established, but perhaps a few may live long enough to give us the answer to this question.

The assistance of Miss Harriet Amory and Miss Janet Murphy in this work is gratefully acknowledged.

SOME OBSERVATIONS ON CHRONIC ARTHRITIS.

By GEORGE DRAPER, M.D.,
NEW YORK.

No attempt will be made at this time to discuss the classification of chronic arthritis. Certain features of the disease and of some individual characteristics of its subjects will, however, be brought out for consideration. The study was developed along lines suggested by the writer's[1] experiences in the poliomyelitis epidemic in 1916 and later among the meningitis cases in the army. These experiences brought out undeniably the circumstance that there was in both diseases a remarkable uniformity in certain anatomic characteristics of the patients. The attempt to analyze this similarity in appearance by comparing each person with a "normal" was unsuccessful, because in a mixed race the normal is quite indefinite. Consequently, recourse was had to the known endocrinopathies.[2] Each patient was observed with an eye to his possession of anatomic or physiologic characteristics which, though slight, might find counterparts in one or other of the endocrine disorders.

The great frequency of the disease arthritis in women is well known. Furthermore, it is often recorded that at the time of the menstrual period patients with chronic arthritis suffer either an exacerbation of their joint symptoms or are very much better. Many cases during pregnancy lose their joint pains about the fourth month. In addition to these observations the menstrual history of women with chronic arthritis describes irregularities of one sort or another; delays, periods of amenorrhea and frequently much pain.

While a considerable number of cases begin with large joint involvement the small joints of the hands have been the target primarily, and often, indeed, comprised the chief articular expression of the malady in its milder forms. The changes in the joints of chronic arthritis have been divided into two main groups, productive and atrophic, but radiographs show clearly that whether joint destruction, which is the criterion of the atrophic form, be present or not there is always increase in the bony structure. This expresses itself as an increase in the bone about the joints, often thickenings in the phalangeal shanks and especially in the terminal tuftings. These important structures assume an appearance extraordinarily like that seen in cases of pulmonary osteoarthropathy. It is also analogous to the appearance of the terminal tuftings and the phalangeal shank thickenings that are present in the well-known radiographic picture of the hand of the acromegalic. It may be well

[1] Draper, G.: Acute Poliomyelitis, Philadelphia, 1917.
[2] Draper, G.: The Relationship of the External Appearance of the Body to Disease, New York State Med. Jour. (not yet published).

to call attention here to the tendency of acromegalics to chronic bronchitis, bronchiectasis and emphysema—conditions which have been associated in turn with the terminal phalangeal changes known as pulmonary osteoarthropathy. Wright[3] reports one case of chronic bronchitis in which pulmonary signs ceased completely when the joint symptoms began, and another case in which the appearance of rales in the lungs was coincident with the onset of arthritis. One other feature which must be mentioned here in relation to the skeleton of these cases is found in the bones of the skull. Here in all five cases were found marked irregularities in the sella turcica (especially thickenings of the posterior clinoid process), all concerned with increased bone-production and an evident increase in the size of the sinuses or the density of the bone structure in the acral portions of the skull. In this connection it is of interest to record the report by Wright of a case of chronic headache which later developed chronic arthritis. The headache ceased with the onset of the joints.

The study of patients with chronic arthritis along the line of comparison with the anatomic characteristics of acromegalics brings out certain points of similarity in other parts of the body almost as striking as those found in the hands. In the five cases on which these preliminary remarks are based the modelling about the brow and eyes, facial bones and jaw is analogous to that of the acromegalic, to wit: prominent glabella region and supra-orbital ridges, high nose bridge and dental irregularities. All the individuals likewise showed a wide subcostal angle and in the male subject a tendency to the feminine distribution of fat and hair. The examination of the blood in these patients also shows consistently a tendency to low total leukocyte count, with the polynuclears diminished at the expense of mononuclear elements, a phenomenon commonly found also in the acromegaloid and Froelich types.

Previously more attention had been given to the thyroid gland in relation to chronic arthritis, especially by the French. Vincent[4] states that 68 per cent. of acute rheumatic fever have thyroid swelling, and believes that those who subsequently develop arthritis deformans have an associated, perhaps residual, insufficiency of the thyroid. The cases of our series have certain anatomic and physiologic markings, suggesting thyroid disturbance, such as dry skin, sweating palms, poor nutrition, nervousness and fatigability. Paul Claisse[5] has also reported the general "slowing down" of all functions in certain forms of chronic arthritis.

The sugar metabolism function of these individuals demonstrates

[3] Rheumatoid Arthritis, Canada Lancet, Toronto, 1911, lxv, 812.

[4] Rheumatisme et opotherapie thyroïdienne, Soc. méd. de hôp. de Paris, 1908, xxv, 677.

[5] Rheumatisme thyroïdien chronique, Soc. méd. de hôp. de Paris, 1908, xxv, 675.

an average or slightly diminished tolerance. In two of the cases there has been a very definite dull frontal headache following the ingestion of sugar. Several of the patients have shown a great craving periodically for candy, after eating which they developed a dull frontal headache. One patient, a male, with spondylitis, is a chronic candy fiend. An examination of the blood count following the ingestion of the glucose for the sugar-tolerance test shows no disturbance of the leukocyte count, except possibly a slight tendency to depress the total count. Several of these patients have described suffering from hives in childhood and occasionally in later life.

The cases of this series, each of which had been "through the mill" for many years in attempts to arrest or cure the disease, have recently been treated in desperation by the old and homely method of the stings of honey bees. While certain definite clinical improvements have supervened in these patients, some interesting observations about the effect of bee stings have been made. It is the chief concern of this report to consider the phenomena associated with the action of the bee venom rather than to discuss its therapeutic effects.

In the first place the bee sting produces a lesion locally which is the perfect replica of an urticarial weal; later on there is generalized diffuse swelling, with redness and heat, and pain and stinging sensation which resemble the lesion of acute rheumatic fever. In two cases it was observed that fading or almost healed sting reactions on one arm, of several days' duration, developed fresh erythema and swelling within a few hours after new stings were given on the other arm. In one instance, on the seventh day following the first stings, there arose about the site of the more recent lesions typical urticarial rose-pink blotchy eruptions. In addition to this the patient had a rise of temperature, with tenderness and swelling of the lymph nodes, the whole picture typical of a mild attack of "serum sickness." Adrenalin injected at this time caused the eruption on the arm receiving the drug to subside. But the eruption on the opposite arm, like the other symptoms, was uninfluenced. Medical literature contains numerous reports of severe symptoms and even death caused by the stings of bees. There is a striking uniformity in all the accounts. In practically every case acute and rapidly advancing swelling, syncope, weak pulse, oppression of breathing and often vomiting supervening, the edema may reach an extreme degree. No better descriptions of angioneurotic edema can be found than in these ancient records of the remarkable phenomena produced by the stings of bees and hornets. It is interesting that every case in which serious or fatal symptoms developed was stung on the face or head. At this point it is worth while calling attention to the reported chemical analysis of bee venom. Much work has been done both by J. Langer and more recently by F. Flury. The former author considers the venom an organic base precipitated by

alkali, giving alkaloidal reactions and remaining undisturbed by heat up to 100° C. Flury has carried the analysis of this base further and finds it to be a complex substance in which an indol derivative isolated as tryptophan, various fatty acids and bodies resembling saponin and lecithin have been found. None of the substances described are usually associated with the phenomena of sensitization and anaphylaxis, so that there seems for the moment to be some discrepancy between the biologic effects of bee venom

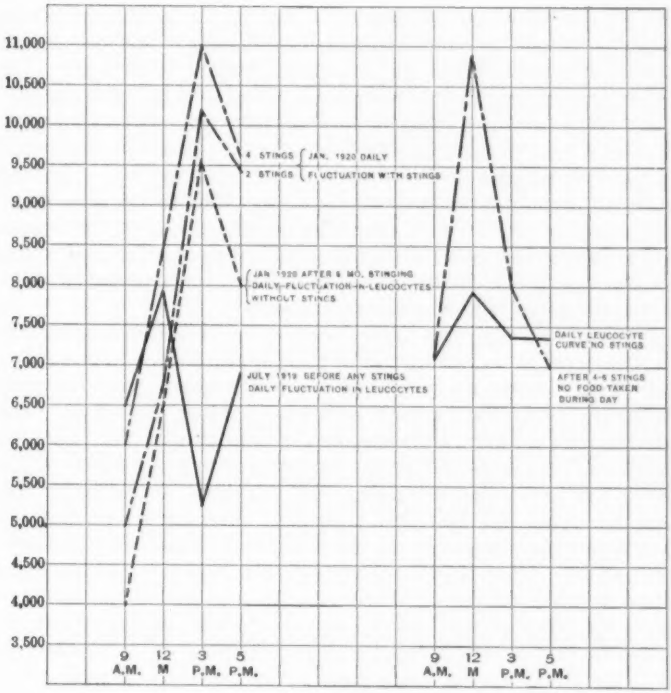

CHART I

and its chemical composition. Langer's work on the hemolytic power of bee venom and its ability to produce local necrosis exposes an analogy to certain snake venoms.

The white cell count of the blood showed interesting changes following the introduction of bee venom. Chart I shows the response of leukocytes to the venom in two cases. In the first case the solid black line indicates the diurnal curve obtained from counts taken at 9, 12, 3, 5 o'clock, before the patient received any venom. The dotted line shows the diurnal curve six months later, after

many stings and definite clinical improvement, on a day when no venom was given. The dash-dot curves show the immediate effect of the venom. In the second case the solid black line represents the diurnal curve taken at some time during the first two weeks after starting bee treatment. The dash-dot curve shows the extreme rise of the count immediately following six stings. All these counts were controlled, with special reference to the time of taking food and on the days from which the charts of the second case were taken the patient fasted all day. Very many observations were made during the year and all confirmed the fact that within fifteen minutes to half an hour after the introduction of the bee venom almost every case began to show an increase in leukocytes. The rise continued sharply for an hour or two and then fell off as rapidly. Some cases showed a delay of several hours before the rise set in. The total count is chiefly elevated, but there is also a definite increase of the polynuclears at the expense of the lymphocytes. This rise of the total count is not sustained but falls within two or three hours to the original level. Over a period of months, however, there seems to be slow, continuous and evenly sustained rise of the total count. In one case in which the bees were omitted for a period of three weeks the count fell back to its original level.

Clinically all the cases have shown a very definite improvement in their sense of well-being and in their appearance. In one case a menstrual disturbance which had frequently amounted to complete amenorrhea for as long as eight months completely cleared up. The periods were resumed and continued at normal intervals. Chronic puffiness of the eyes and ankles disappeared and the effect on the joints was also very noticeable. The subjective improvement was marked. One case had dull headaches following stings, but the joints were less affected by atmospheric changes than they had been previously. All of these patients were old stagers in the matter of knowing what real improvement was, and had been disappointed so often that they started out as complete skeptics, so that whatever value there may be in subjective improvement in the matter of pain and discomfort is worth more in this particular malady probably than in some others.

Just what the mode of action of the bee sting is at present is comparatively obscure, but the effect upon the blood count, the skin reactions and the reports of generalized edema and the temperature rise suggest acute protein shock analogous to the effects obtained by injections of many foreign proteins. Artificial bee stings composed of various dilutions of formic acid produce the same, though much milder, local effect than the true bee sting does and no constitutional changes. The indication that sensitization processes are concerned and the consideration of the analogy of the bony changes to those associated with pulmonary conditions led to inquiry for the presence of asthma, urticaria and eczema in the patients

themselves or in members of their families. Chart II illustrates, in striking fashion, the intense predisposition to the disturbances under discussion, which runs through the family tree.

Consideration of all these points leads to the conclusion that chronic arthritis represents a very profound constitutional disturbance in which forces analogous to those concerned in acromegaly

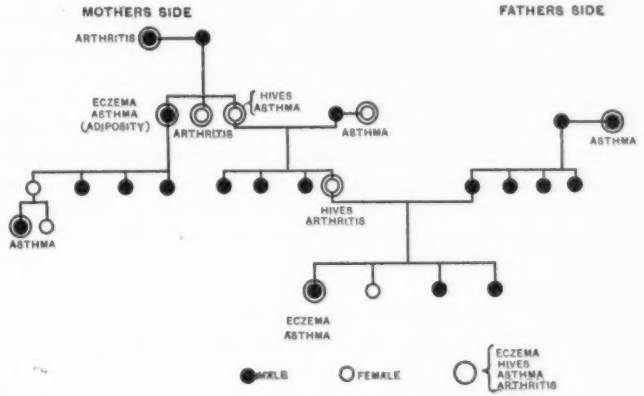

CHART II

and thyroid insufficiency are concerned. The family and personal history which arthritic patients give of hives, angioneurotic edema (bee sting effects) and asthma, and, in addition, the well-known feature of joint involvement seen in serum disease, all seem to indicate that there is a relationship between this whole group of phenomena and chronic arthritis.

INTERPERITONEAL ADHESIONS, THEIR ORIGIN AND PREVENTION.

BY R. J. BEHAN, M.D., F.A.C.S.,
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Three series of experiments on rabbits were made with three different purposes in view:

1. To define the origin and prevention of adhesive formations in the peritoneal cavity.

2. To elicit the active cause of acute gangrenous (suppurative) appendicitis.

3. To determine whether an opening in the bowel, made either by accidental traumatism or during an operation, may be closed

permanently by implanting a portion of another segment of isoperistaltic bowel into the opening, so that the serosa of the implanted bowel is sutured to the mucosa of the bowel at the margin of the defect; the defect is present, making as it were a plug to block the opening.

I shall confine this paper to a discussion of interperitoneal adhesions as produced artificially.

By experimental methods an attempt was made to produce interperitoneal adhesions: (1) By chemical irritation; (2) by traumatism of the serosa surface of the peritoneum; (3) by the action of bacteria or of sterilized cultures of bacteria (bacterial toxins).

After attempting to define which of the above processes was potent to cause adhesive formation, further effort was made to determine the extent to which adhesions could be restricted or inhibited by the application of lanolin and boric acid (5 per cent. boric acid in lanolin). By previous experiments it had been shown that this preparation had a restrictive action on the formation of interperitoneal adhesions.

It was also determined by the present series of experiments that in the presence of normal inflammatory tissue reaction the result of bacterial invasion, that lanolin and boric acid does not prevent adhesion formation. The cause of such failure evidently is that normally when the serosa is irritated by chemical means or is superficially destroyed by traumatism the lanolin and boric acid paste applied over the affected area acts as a protection to these areas for several hours, or until sufficient time has elapsed for the normal protective forces in the affected area to renew the serosa to such an extent that adhesions cannot be formed. If the serosa destruction is not repeated new endothelium forms and no adhesions form. However, if repeated destruction of the endothelium occurs at short intervals or if the destruction is continuous, as in inflammatory reactions, the protective action of the lanolin and boric acid does not continue sufficiently long for the new endothelium to form.

For adhesive formations between two adjacent areas of the bowel, or between the bowel and some other viscera or the peritoneal coating of the abdominal cavity, it is necessary that both opposing surfaces be denuded; or, if the two surfaces coming into contact with each other are not denuded, that they remain in forcible contact for a considerable period of time. How long a period of apposition is necessary I have not been able to determine. If such apposition is present, and if one of the apposing surfaces is denuded or is inflamed, the exudation which forms upon the affected surface will come into contact with the unaffected serosa of the opposite surface and will produce the same reaction in this area as in the affected surface.

If the two serosa surfaces have been injured and are kept in contact it requires only a very short period of time for adhesoin formation to take place. However, if neither of the two adjacent surfaces is injured, or if there is no inflammatory exudation present in the immediate neighborhood, adhesions will not take place between these two surfaces.

Chemicals such as tincture of iodin, carbolic acid, Dakin's solution, bichloride of mercury in strong solution, etc., will quickly destroy the frail endothelial cells on the serosa surface. Even when two adjacent surfaces come into direct contact and the serosa has been destroyed or injured, union will not take place if there is sufficient movement between the two apposing surfaces to inhibit a direct and intimate contact for a considerable period of time does not ensue. Exposure to the air, so that the serosa surface of the intestine was thoroughly dried before the bowel was returned into the abdominal cavity, did not cause adhesion formation (experiment of September 19, 1917).

Therefore from the experiments we have conducted it has been considered best, after operation in which considerable traumatism to the serosa surface in the abdominal cavity has occurred, to frequently change the position of the patient and at the same time to give some drug, such as eserin, which will stimulate the peristaltic activity of the intestine. Tympanites should be counteracted immediately. Heat instead of ice should be applied over the abdominal cavity.

As confirmative of the above opinions I shall review a few experiments in which an attempt was made to cause interperitoneal adhesions, and then after having determined that adhesions could be formed under certain conditions, I shall detail the results of attempts made, under similar conditions, to inhibit the formation of adhesions by the use of a heated paste of 5 per cent. boric acid in pure lanolin.

In these experiments it was noted that when inflammation was present in the peritoneal cavity that the lanolin had a tendency to collect in small, whitish masses and that adhesions would form the same as though lanolin had not been used.

This is exemplified in an experiment of February 4, 1918, when a small needle opening was made in the end of the appendix of a rabbit and some of the appendicular contents was expressed upon the surface of the appendix. Tincture of iodin was now injected into the appendix and also was applied to the appendix over the needle opening. This portion of the appendix and the adjacent structures were now covered with lanolin and boric acid.

At an operation performed on February 12, 1918, it was found that the appendix was inflamed, very red, with numerous adhesions at the extreme tip. They were very firm and extended for a short distance. The adhesions were freed and bled profusely. This

experiment should be compared with the one in which it was demonstrated that lanolin and boric acid applied in the absence of fecal contamination, over two adjacent surfaces to which tincture of iodin has been applied, can prevent adhesions. This protective action was demonstrated by the following experiment:

In a rabbit on February 4, 1918, tincture of iodin was mopped on the mesocolon to the left of the large colon. Lanolin and boric acid were applied over this area. At an operation on February 12, 1918, it was found that the area of the mesentery and bowel to which tincture of iodin had been applied and over which lanolin and boric acid had been smeared was free from adhesions. Tincture of iodin and lanolin and boric acid were again applied to this area. One month later the rabbit was again operated and it was found that adhesions were very marked over the entire abdominal cavity. It was also noted that there were masses of whitish material present in the abdominal cavity, collected mostly on the right side. Evidently the aseptic technic had been defective in this case, and inflammation, protective in type, had taken place, thus conserving the life of the rabbit. The lanolin and boric acid had not inhibited this protective inflammatory reaction.

The results in the above cases are confirmative of the results obtained in earlier work.[1]

In an experiment performed on December 25, 1917, two adjacent surfaces of bowel were swabbed with tincture of iodin, full strength. Approximation sutures were now placed so that the two surfaces were held directly in contact. No lanolin nor boric acid was applied. On December 28 the rabbit died from an acute inflammation, induced by artificially produced appendicitis. It was found that the areas of the bowel which had been treated with tincture of iodin and had been approximated were slightly adherent to each other. In another rabbit two adjacent surfaces of the bowel were denuded of their serosa by rubbing with the edge of a knife-blade, and over this lanolin and boric acid were applied, after first swabbing the abraded surface with tincture of iodin (full strength). The adjacent surfaces were found on December 25 to be adherent to each other at the lower end of the denuded area, beyond the area over which the lanolin and boric acid had been applied. The experiment added further proof of the potency of the lanolin and boric paste to inhibit adhesive formation, as the experiments show that tincture of iodin will cause dense adhesions when the bowel surfaces are held immovably in contact by suture and that lanolin and boric acid will retard adhesive formation even when the adjacent surfaces are denuded and tincture of iodin is applied.

The experiment of January 19, 1918, is further proof of the activity of tincture of iodin as a cause of adhesive formation.

In this rabbit tincture of iodin was applied to the serosa surface

[1] Report in New York Medical Journal, July 22, 1916.

of the mesentery of the large bowel and to the adjacent segment of the bowel. The viscera were then pushed back into the abdominal cavity on the left side and were covered with other bowel segments, so that the operated area was entirely separated from the wall and the appendix, which had been operated on at the same time. It was found on reoperating, February 10, 1918, that at the place where the tincture of iodin had been applied adhesions were so firm that it was necessary to cut them. There was considerable bleeding from the raw surfaces. The above experiment indicates that adhesions readily occur when two adjacent serosa surfaces of the bowel are irritated by chemical means and are then kept in contact. At this stage of our inquiry a very pertinent question to be answered was, Will direct and immovable contact of two serous surfaces, in the absence of traumatic or clinical irritation, be sufficient to cause adhesions? The result of such a contact is shown by an experiment of April 13, 1917. Two segments of bowel were sutured together so that a small pocket was present between them. On April 18 no adhesions were found except where the sutures had joined the two surfaces of the bowel together. At another place two adjacent surfaces were approximated, but into the pocket formed by this approximation three or four loops of a killed culture of colon bacilli were introduced; there was a slight amount of bleeding. It was found on April 18 that adhesions were present. Adhesions were also present in another case, where three or four drops of a killed culture of colon bacilli had been inserted into a pocket formed by approximating two serosa surfaces. Lanolin was also applied in this case and there were dense adhesions. Dead bacteria apparently are active in inciting adhesive formation. This is also shown by an experiment in which in one place several drops of colon bacilli were inserted where the bowel formed a loop and a pocket was present. On June 20, 1918, it was found that there had been present in this area a very severe reaction. In the entire lower part of the area were found dense adhesions, which could only be separated by cutting. Dead colon bacilli injected into the peritoneal cavity are very toxic, as is shown by the following:

One cubic centimeter of a three days' culture of colon bacilli, a subculture of the colon bacilli used in the above experiments, was injected into the peritoneal cavity of a rabbit. The dead bacilli were diffused around the peritoneal cavity by means of the fingers. The rabbit died suddenly in four hours.

In a rabbit operated April 28, 1917, an attempt was made to define the reaction following denudation of both sides of the adjacent serosa surfaces, and the smearing of lanolin and boric paste over the denuded areas. This paste, however, had hardened and did not make a perfect film. The abdomen was then closed. On June 16 there was a firm union between the two adjacent surfaces. In this instance the lanolin and boric acid had been hardened and did not

make a perfect film, and this apparently accounted for the adhesion formation.

In another place in the same rabbit, on April 28, two bowel surfaces were rubbed rather severely with gauze, but not severely enough to cause bleeding. The adjacent surfaces then were approximated and held in contact by linen sutures. No lanolin was used. Firm adhesions resulted and were found in the operation of June 16. However, there were no adhesions to the adjacent viscera.

To further define the tendency to adhesion formation an operation was performed November 6, 1917, and the adjacent surfaces of two segments of the bowel were brought together at *A*, but were not denuded. At *B* they were denuded of their serosa on one side and at *C* they were denuded on both sides. At *A* and *B*, two days later, no adhesions were formed, but at *C* both surfaces were adherent.

This experiment was a repetition of one performed on September 29, 1919. At this time three areas were approximated. In one neither of the two adjacent serous surfaces was denuded. In the second area only one was denuded. In the third area both surfaces were denuded. However, in this case there was a considerable deposit of blood between the two surfaces, due to perforation of a vessel in the serosa of the bowel. On reoperation, September 14, 1919, it was found that the bowel had become adherent to the abdominal wall. On attempting to remove it it was perforated in several places. The entire abdomen was contaminated with feces. The cause of the adhesion probably was an infection with streptococci, a very active culture of which had been injected into the appendix at the time of the prior operation. On eventrating the intestines it was found that the approximated bowel surfaces were very firmly adherent, except at the point where neither of the two adjacent surfaces had been denuded of their serosa. Even here, however, there were numerous fine adhesions. It was impossible to separate the two adjacent surfaces of the bowel in the other two areas.

This would indicate either that there had been infection from streptococci or else that the presence of blood between two adjacent surfaces had a tendency to cause the serous surfaces to unite to each other. The latter apparently is the most probable, because in this experiment the rabbit had no adhesions present in the peritoneal cavity, except in the area where the bowel had been interfered with and near where the abdominal incision had been made. If there had been a bacterial destruction very likely a generalized peritonitis would have occurred, and adhesions would have been present throughout the entire abdominal cavity.

Another rabbit was operated on November 19, 1919. The same procedure was carried out as in the previous rabbit, with the exception that lanolin and boric acid were introduced between the adjacent

surfaces. In this rabbit there was also an operation on the appendix. The rabbit died the next day because of a gangrenous appendix. There was a considerable amount of inflammatory reaction in the abdomen adjacent to and around the area where the bowel surfaces had been approximated. All the bowel surfaces were found to be adherent to each other. These adhesions were evidently the result of inflammation.

In a rabbit operated on October 11, 1919, two segments of the large bowel were approximated by sutures. The space between the two segments was now covered with tincture of iodin (3½ per cent. strength) and the bowel was reintroduced into the peritoneal cavity. Some of the surface, which was covered with tincture of iodin, was permitted to come into contact with the lateral peritoneal wall, the iodin being spread considerably over the surface of the bowel. Five days after operation it was found that there were a few adhesions present between the bowel where it had been approximated by sutures. It was noted that while iodin had been spread over the two adjacent surfaces to a considerable extent, beyond the place where they had been approximated, the union between them had only taken place where they were approximated, and that it had not occurred between the lateral peritoneal wall and the surface of the large bowel, which had also been covered with tincture of iodin. In this case it was also noted that adhesions between the incision in the abdominal wall and the mesentery had been more pronounced than between the incision and the serosa of adjacent bowel. There also seemed to be some adhesions between the mesentery and the portion of the bowel which had been covered with tincture of iodin, so that one might conclude that the tendency for tincture of iodin (3½ per cent.) spread upon both adjacent surfaces, with the bowel held in intimate contact so that it cannot move away, is to destroy the serosa.

However, when the bowel is freely movable and when it does not remain in permanent contact with the peritoneal wall, adhesions do not take place between it and the adjacent peritoneum. From this experiment it would seem 3½ per cent. tincture of iodin should not be used in the abdominal cavity unless it is desirous to promote adhesion formation or unless two adjacent areas of bowel so treated can be kept separated.

As noted above, lanolin and boric acid had a tendency to inhibit adhesions when tincture of iodin had been applied. Lanolin will also inhibit adhesions when an intestinal anastomosis has been made, as exemplified in the rabbit operated on June 20, 1917, in which an opening had been made into a segment of the bowel. Into this portion another bowel segment had been sutured. On operation, November 6, 1917, no adhesions were present around the place where the bowel had been inserted into the lumen of a second segment of bowel.

From the above experiments it may be concluded that lanolin and boric acid tend to inhibit adhesive formation only in cases in which there is no inflammatory reaction present. The inflammatory reaction inhibits the potency of the lanolin and boric acid. Lanolin and boric acid will not always inhibit adhesive formation where two adjacent surfaces are kept in intimate and permanent contact after they have been denuded of their serosa. Also, in case blood is present between the two adjacent immobile surfaces, lanolin and boric acid will not prevent the formation of adhesions. Nevertheless, from the very fact, that lanolin and boric acid inhibit adhesive formation in most cases of minor traumatism to the peritoneal surface, also in cases of more severe traumatism where there is more or less free movement of the intestine (abdominal viscera), and in other cases where no inflammatory reaction has taken place, it seems that the lanolin and boric acid performs a very valuable function, and should be used in all cases in which interperitoneal adhesions have been separated and in other cases in which it is thought possible that adhesions may form. As a further means of prevention it should be so arranged that two raw peritoneal surfaces do not remain permanently in contact with each other.

Summary. I have used lanolin and boric acid in over three hundred abdominal sections and have noted no bad results from its use. In fact, patients after its use claim they have very little pain, and those who have had a previous abdominal section and are able to compare their sensations with those experienced after the previous operation are always pleased with at the greatly lessened pain which they experienced when lanolin and boric acid had been used. For this reason, *i. e.*, the relief of pain alone, the use of lanolin and boric acid is justified. It certainly produces greater ease in the very severe operative patients. I find it very beneficial in those patients who have developed adhesions around the cecum and ascending colon, either from a chronic appendicitis or as the result of some congenital defect by which stasis is present in the colon, and has resulted in a perityphlitis and pericolonic adhesive formation. In such patients I use it very liberally and have had uniformly good results. I have also used it in several cases of recurring interperitoneal adhesions with gratifying absence of the former symptoms.

The presence of adhesions between the omentum and adjacent vsicera or the omentum and the abdominal wall, where a previous operation has been done, is also a suitable indication for the use of lanolin and boric acid.

In using lanolin and boric acid, however, precaution must be taken that the lanolin secured is as nearly pure as possible. Most of the lanolin on the market is contaminated in various ways and frequently its interperitoneal use causes a very marked reaction, *i. e.*, an elevation of temperature and of pulse. It should also be sterilized three times on three different days, each time for a half hour at a

temperature of over 212°. Before being used it should be heated so that it is absolutely fluid; in fact, it should be applied very hot to the peritoneal surface. In this way it dries out the moisture of the peritoneum and at the same time sticks very firmly to it. It should not be applied upon a moist surface. The bowel should be dry before its application.

I have also used lanolin and boric acid rather successfully in tendon implantation and transference, also in cases in which it was necessary to liberate tendons from adjacent structures, the adhesions being due either to traumatism or to tenosynovitis.

I have been using this preparation for the last five years. I am very well satisfied with it, and feel that it does a great deal of good.

Lanolin and boric acid paste, of course, has its limitations, as I have stated. In the presence of inflammation it does not act. This is a valuable quality, because if it did inhibit adhesions, in cases of peritoneal inflammation, its use would be very dangerous. Adhesions are the life-saving structures in inflammation of the peritoneum. Another fact of importance to be remembered is that lanolin and boric acid paste does not absolutely inhibit adhesions between two adjacent surfaces, which are denuded of their serosa and are held in contact. Therefore, it should be the attempt of the surgeon to see that no two surfaces denuded of serosa come into and remain in permanent contact. The viscera at the close of an intra-abdominal operation should be so arranged, if possible, that long contact cannot happen, and, as a further precaution, the position of the patient should be such after operation that involved peritoneal surfaces will have a tendency to gravitate away from each other, for this reason also the position of the patient should be frequently changed. Drugs which have an active peristaltic action, either strychnine or eserin salicylate, should be exhibited in quantities sufficient to produce active peristalsis. Magnesium sulphate is also a very good drug, useful for this purpose. Any cathartic, stimulating intestinal peristalsis may be exhibited with profit.

As a further aid to peristalsis, where there is no danger of spreading an inflammation, we apply heat to the abdomen in the form of hot-water bottles, electric pads, etc., which are very beneficial in sluggish peristalsis. Diathermia is one of the most recent but perhaps one of the best means of stimulating peristalsis after operation.

THE PRESENT STATUS OF EMPYEMA.

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In this communication only those cases of empyema thoracis will be considered which are caused by the common pyogenic organisms —streptococci, staphylococci, pneumococci, etc.—and which follow most frequently ordinary pulmonic inflammatory conditions. An entirely different problem is presented when the lesion is due to other inciting organisms, such as tubercle bacilli or actinomyces.

In 1915[1] some studies on empyema thoracis were completed and published. The conclusions which were brought out at that time have since been abundantly corroborated, and some of them seem to have acquired much additional significance. It is of importance to recapitulate the latter and to compare them with our added knowledge.

"In the vast majority of the cases empyema is secondary to some other inflammatory lesion in the body." Approximately 11 per cent. of the cases in the 1915 series were described as being "primary" in the pleura, and the most predominating reason for the assumption was that it was not possible to demonstrate at any time the primary lesion to which the pleural suppuration was subsidiary.

The opportunities afforded by postmortem* examination do not always lead to an accurate opinion concerning the mechanism of the early stages of the pleuritis. Except in those cases in which section of the lung demonstrates consolidated areas in anatomical relationship with the diseased area of the pleura, there are no criteria present upon which any judgment can be based. In the greatest number of the ordinary† cases of suppurative pleuritis the pathology, as demonstrated at autopsy, includes a localized intrapleural abscess of larger or smaller extent, bounded by thickened parietal and visceral pleural layers, on the pulmonary side of which the lung tissue shows no change from the normal, or only such superficial inflammatory, or compression, changes as would naturally be expected in a structure in direct and intimate anatomic

* No conclusive evidence can usually be demonstrated at operation regarding the priority of the lung or pleura in a pathological process in which both are implicated.

† The extraordinary conditions are, of course, those associated with epidemics. In a subsequent part of this communication the streptococcus cases which formed a fairly large proportion of the cases in the last influenza epidemic will be discussed. I have the impression that outbreaks of primary streptococcus pleuritides which affect relatively large numbers of people have been known unassociated with any "influenzal" epidemic.

relationship with a pyogenic process; these are the comparatively late cases. Such findings are expected in the primary pleuritis cases, but could equally well occur in the cases in which a pulmonary condition had antedated the pleuritis and in which, prior to the time the examination was made, healing of the lung lesion had been completed and had been accompanied with the disappearance of any perceptible evidence of the original anatomic changes; this state of affairs, I am quite sure, is very common.

Apparently a primary pleuritis can occur in one of two ways: One of the two, and perhaps the much less common, consists of an absorption of bacteria by the lymphadenoid tissue of the lung from the inspired air, with a consequent reaction in the pleura alone. Evidence toward this assumption was presented by Grawitz,[4] Arnold,[1] Heller[5] and Netter[8] in the period from 1890 to 1897, but since that time no additional proof of any kind has appeared in the literature. My own studies have led me to believe that under ordinary conditions this mechanism must be an exceedingly rare one, if it ever operates at all.

The second mechanism concerns itself with the phenomena associated with a temporary bacteremia. Organisms find their way into the blood stream, having gained an entry through the respiratory (including tonsils and adenoids), gastro-intestinal or genito-urinary tracts; and for some reason, which may not be apparent at any given moment, the pleura forms a fixation-point for the bacteria as these are filtered out of the circulating blood and an empyema results. Probably this mechanism functionates with many other similar or allied conditions; very possibly, too, it operates in the first of these two methods. Under such conditions it is very likely that the responsible organisms show an elective affinity for the pleural membrane. At the present writing it seems to me that no other available theory is adequate to explain the almost simultaneous occurrence of relatively enormous numbers of cases of primary pleuritis under epidemic conditions.

Over 90 per cent. of the empyemata one meets with are secondary to other immediately preceding conditions. It cannot be overemphasized how important this observation is. In this respect the term empyema holds an exactly parallel place with the term peritonitis: neither of these expressions conveys a total concept to the clinical mind unless it be immediately modified by an indication of the primary inciting condition. The primary conditions can be roughly grouped into (1) the meta- or postpneumonic empyemata; (2) those occurring by continuity from a neighboring perforating abscess, and among these abscesses of the lung take first place; and (3) the metastatic forms following a focus of suppuration at a distant point or taking the form of fixation abscesses in the course of established and continuing bacteremias.

1. The empyemata with which one meets most commonly are those following pneumonia. In children a form occurs in which both pleura and lung simultaneously become infected and involved. In adults this form is rare, and, as far as one can tell, the usual course of affairs includes a definite progression from a pulmonary inflammation to a pleural involvement. Rosenbach[13] was the first to suggest the probability that many of the meta- and postpneumonci empyemata are directly induced by the rupture into the pleural cavity of small superficially placed pulmonary abscesses resulting from foci of liquefaction in the consolidated portions of the lung. The difficulties in adequately settling this point, especially as to the frequency of its occurrence, are apparently insurmountable; but what evidence we have seems increasingly to show that this mechanism is perhaps the most common, if not the only one, by which the ordinary forms of meta- and postpneumonic empyemata make their appearance. In a number of instances I have been able to demonstrate these abscesses on the operating table. One of these was in a fresh case of empyema; the other was found during the course of operation for the closure of an old thoracic fistula: in both of these in exploring the visceral surface of the empyema cavity the finger was caught in a small round hole which led into the pulmonary parenchyma. The observation of Rosenbach[13] is also corroborated in the report of the U. S. Army Empyema Commission[3] in the cases which occurred at the camps during the epidemic, small abscesses, which often were multiple, were repeatedly found at autopsy in the lungs, gathered at their peripheries and directly under the visceral pleura.

These cases should not be conflicted with any of the forms of empyema in the second group—empyema cases complicating frank pulmonary abscesses.

Meta- and postpneumonic forms of empyema form about 69 per cent. of the total number of cases encountered.

2. About 2 per cent. of the empyema cases under ordinary circumstances complicate abscesses in the immediate neighborhood of the pleura. This group includes only those which are formed by direct extension or rupture of the suppurative process. Very few of these, indeed, are derived from the subdiaphragmatic space; the very largest number are derived from the rupture of pulmonary abscesses. The latter form an important group of empyemata. The mechanism in these cases is quite simple, and it is possible to distinguish two varieties. In one of these there is a comparatively acute abscess formation with soft, non-demarcating walls, frequently multiple, commonly with few or no physical signs, and very liable to cause perforations between the non-adherent visceral and parietal pleuræ; the latter accident becomes associated with a sudden increase in the severity of the symptoms and the clinical picture becomes associated with, and characterized by, high fever, marked dyspnea

and cyanosis and other signs of a high grade of intoxication. The picture is that of a hyperacute pneumothorax. Pathologically these abscesses are noted by the absence of surrounding areas of induration. The resulting empyema involves, practically, the entire pleural cavity; the exudate is distinctly purulent, rather thin and frequently sanious, very foul and very toxic. As far as I know almost every case of this kind goes on to a fatal issue.

The second variety includes the chronic lung abscesses. The most characteristic of these are the foreign body intrapulmonary suppurations which follow aspiration of a fragment of tonsillar tissue during a tonsillectomy. Anatomically the lesion consists of a central cavity containing foul-smelling, brownish-red, grumous pus in which a multitude of organisms flourish; a limiting granulation membrane of firm consistence and a wide surrounding area of induration merging into pulmonary tissue in which fibrosis, secondary bronchiectatic dilatation and atrophy predominate. The lesion may be single or multiple and with it an advanced grade of suppurative bronchitis is associated. An adhesive pleuritis is almost the rule and is usually limited to the area of lung involvement. Empyema is less common; a general empyema is rare and occurs in those very exceptional cases in which no pleural adhesions have formed. The empyemata which are found are comparatively small and localized and the mechanism of their production becomes apparent from the anatomic structure in which one wall of the cavity is formed by much thickened parietal pleura and the opposing wall by suppurating membrane based on pulmonary parenchyma (pleural vomica). A bronchial fistula is always present. Clinically these are characterized by a prolonged period of illness, by a distressing cough, by fetid and profuse purulent sputum, by the evidences of progressive general deterioration and of local pulmonary involvement, and by characteristically definite roentgenographic pictures.

This type of empyema is illustrated by the notes of the following case:

In a man, aged fifty years, a lobectomy was done for a chronic lung abscess. The description of the pathology, as demonstrated at operation and by study of the specimen removed, is as follows: The lesion was present in the lower right lobe. The anterior, mesial and diaphragmatic surfaces of the lobe are free from adhesions. The latter are, however, present at the postero-internal border of the lung as far forward as the ligamentum latum pulmonum and for the entire extent of the latter from the pulmonary hilum to the base. In this location there is an empyema cavity containing several ounces of thick, yellow pus. The mesial wall of the abscess was a much thickened parietal pleura lining the reëntrant angle formed by the bend of the ribs and posterior mediastinum; the outer wall was pulmonary parenchyma in which the open ends of a number of bronchi of the second and third order were easily and distinctly

visible. The empyema lay for the most part within pulmonary parenchyma.*

The demonstration of a bronchial fistula furnishes indubitable evidence of the presence of a suppurative process in the midst of the lung tissue. In the great majority of such cases the presence of the fistula is to be interpreted as proof of the priority of the pulmonary process, to which the empyema is subsidiary. In the lung-abscess-empyema cases the communication is frequently multiple, is usually direct and extends almost always into one or more fair-sized bronchi of the second or third order; the usually profuse and foul sputum, present before operation, resembles in all particulars the pus of the abscess; but it immediately disappears following the adequate drainage of the pulmonary abscess and reappears directly the drainage is interfered with from any accidental or purposeful cause. Healing is tedious and prolonged, and most often the bronchial fistula is an insurmountable obstacle to the closure of the thoracic sinus until, and perhaps even after, a radical operation is done. In those empyema cases which are subsidiary to the small superficial pneumonic abscesses (Rosenbach[13]) that rupture into the pleura a communication with the bronchial tree is not always demonstrable; in much the smallest number a communication makes itself apparent when, for one or another reason, a fluid irritating to the respiratory tract is introduced into the empyema cavity. The fistula may be tortuous and is narrow, and communicates usually with one of the smallest-sized or terminal bronchi. The amount of infiltration around the sinus tract is at a minimum, the tissues are soft and pliable and have a tendency to fall together; facilities for healing are most favorable in these cases, and it is exceptional for the communication to cause any extraordinary prolongation of the cicatrization of the wound. Characteristically the amount and physical appearances of the sputum is independent of the contents of the empyema cavity, has no resemblance to the wound discharges and depends for its production on any associated bronchitis which may be present or upon the liquefaction of the pneumonic exudate which had antedated the empyema.

In only a minority of the cases of empyema complicated with bronchial fistula is the evidence sufficient to indicate that the communicating sinus had resulted from the rupture of the empyema into some part of the bronchial tree. Such, for instance, would be so when an unrecognized liver abscess perforates through the diaphragm and discharges through a bronchus after having first created a subsidiary abscess in the intrapleural space; these occurrences, while quite well known, are relatively infrequent. With simple empyemata the discharge of pus into the respiratory tract is extremely rare, and probably when such an accident occurs it

* Private records.

indicates the rupture of a coexisting, and perhaps unrecognized pulmonary focus. The experiences which I have had seem to show that the intrapleural abscess discharges much sooner on the skin (empyema necessitatis) or remains practically in an unchanged state except for the progressive thickening and even calcification of the limiting membrane. The prevalent beliefs in regard to accidents of this kind with simple empyemata seem to be exaggerations of the actual facts.

I have, personally, seen only one case in which an empyema ruptured into a bronchus. This was a woman who was admitted into the hospital on the service of Dr. Libman. An empyema was demonstrated and the pus was removed by aspiration as a preliminary measure. Several days later the patient was transferred to the surgical side (Dr. Elsberg's service) for operation; her condition was excellent at that time. As the patient was put upon the table for operation she very suddenly began to show signs of pulmonary embarrassment and within a very few minutes there was a marked edema of the lungs; she was deeply cyanosed and complained of a choking feeling. Under vigorous stimulation she was tided over the emergency and within a few hours began to bring up in the sputum moderate amounts of pus demonstrating beyond question that the purulent focus had ruptured into a bronchus. I believe that a lung abscess was present which had, primarily, caused the empyema, and, secondarily, had ruptured into the bronchus; the presence of the lung abscess had been suspected from the clinical manifestations by the medical men before the transfer of the patient to the surgical side.

It is a different matter with the frank lung abscesses; perforation into the bronchial tree is almost the rule with partial, or complete, drainage of the pus in the sputum.

3. Metastatic empyemata are very common and comprise between 4 and 5 per cent. of the total number of cases ordinarily seen. It is very probable that the mechanism of their production is very intimately connected with the lodgment of infected emboli within the confines of the pleura derived from the original source of infection. It is less common for empyemata to complicate the bacteremias in which no localized focus can be demonstrated clinically; usually there preëxist foci of suppuration from which the bacteria-carrying emboli are derived. The same question arises with these cases as to whether the secondary process in the pleura is primary in the pleura or is in its turn subsidiary to a superficial lung abscess. It seems more rational to assume that the emboli lodge in the capillaries of the lung near the surface and, after liquefaction of the focus has occurred, the latter ruptures into the pleural cavity with the resultant empyema formation. The same difficulties in proving this point are present and in the few cases of this kind which I have had the opportunity of seeing postmortem the stage of the process

was so advanced as to make the elucidation of the question at issue impossible.

Metastatic empyema occurs most commonly after suppurative conditions in the lower abdomen and pelvis—postpartum sepsis, diseased adnexa, suppurative appendicitis; less frequently it follows thrombosed hemorrhoids, middle-ear suppurations or abscesses in other organs. In looking over my records I was surprised to see that I had never observed an empyema to follow a furunculosis.

Unless there is present an established bacteremia the prognosis for metastatic empyema is not any more grave than for other forms of suppurative pleuritis.

Conditions during the epidemic of 1918 and in the various army camps, although peculiar, fitted in with our previous knowledge. The empyemata seem to have followed one of several types.

1. The cases resembling those ordinarily seen and following pneumococcus pneumonias of the lobar type (Alabama drafts at Camp Custer and Camp Upton). The proportion of cases developing empyema was not out of the ordinary and in the Camp Upton cases (Brooks and Cecil[2]) it is put at 11 per cent. The trouble seemed to be that unexpectedly large numbers of the men came down with pneumonia; the pathological lesion itself or the complicating empyema showed no new phenomena.

2. In some of the camps (Camp Custer and Camp Sevier) there were large numbers of men who fell ill with measles. In such closely crowded quarters the measles assumed epidemic characteristics and an unexpected severity. That in turn large numbers of the men, ill with the exanthem, developed pneumonias of various kinds was to be expected; such a progression is common in civil practice when measles spreads in epidemic form in the wards of a hospital, and especially among adult patients. The clinical experience of the camp hospitals parallels that seen in the civil hospitals: the primary exanthem might be mild or severe; the complicating pneumonias were many, were either of the lobar or lobular type, were marked by the evidences of marked toxemia, were frequently complicated by empyema and the total mortality was very high.

In some of the measles cases at Camp Custer (Beals, Marlow and Zimmerman) the pleuritis occurred without any demonstrable preceding lung involvement. In a few of these lung infiltrations were found postmortem surrounding the intrapleural abscesses, but the physical characteristics of these and especially their distribution seemed to furnish sufficient proof of their secondary and subsidiary nature. Some of the cases of empyema following measles, which I studied in the 1915 series, were of this type.

At Camp Upton (Brooks and Cecil[2]) pneumonias frequently followed tonsillitis or other mild infections, and these, in turn, were complicated by considerable numbers of empyemata.

3. The most peculiar cases were those due to the "influenzal"

infection. The clinical pictures were characterized by a fulminating overwhelming of the patient by a tremendous toxemia and in the early stages of the epidemic this was so marked that large numbers of the patients died before any localizing process could form. Then, as the virulence of the epidemic abated somewhat, localizations were made out in the pleura more and more frequently; these assumed the characteristics of pleural effusions. The toxemia was still extraordinary and the patients died before the effusions could become definitely purulent. Very few empyemata were encountered in the early months of the epidemic for these very reasons. Toward the end of the epidemic empyemata began to appear: the virulence of the infection was at its lowest; the patients did not die so quickly; opportunity was afforded for the full development of the pathological process and the longer intervals were conducive to the slow transformation of a pleural effusion, heavily charged with organisms usually of the streptococcus group, into a frank pyothorax. The mortality was still high; the deaths occurred rather early and were due to the initial illness and the character of the infection with its marked toxemia.

Postmortem examinations were frequently disappointing. The pleuræ showed the lesions of fibrinous or serofibrinous pleurisy. The lungs showed patches of bronchopneumonia or the process involved an entire lobe. The bronchopneumonias of streptococcus origin were of a peculiar organizing type and were especially prone to undergo liquefaction and form abscesses (McCallum). Fairly often the lungs were free of any change. These last cases came nearest to the classification of primary pleuritis. Undoubtedly the infection in any case was blood-borne and temporary or more prolonged bacteremias existed to which the pleuræ, or pleuræ and lungs, were points of fixation.

The pleuritis cases of this group have very marked resemblances to similar cases which occurred in previous epidemics. I quote rather freely from Leichtenstern's monograph on "Influenza" in Nothnagel's *System*. "In previous epidemics there were numbers of severe, mostly fatal cases of acute primary 'grippe-pleuritis' which made their appearance almost simultaneously with the appearance of the epidemic. The clinical course began with chills; almost immediately thereafter there was a high, continuous fever, extreme dyspnea and marked cyanosis. In a very short time a rapid accumulation of pleural fluid took place which not infrequently was bilateral. The fluid was thin, turbid, seropurulent and of a yellowish color. In repeated postmortem examinations it was definitely proved that these were primary pleurisies without any coexisting inflammatory infiltration in the lungs. In the exudates streptococci were often found in pure culture. As the virulence of the infection subsided empyemata became frequent."

Exploratory Aspiration. In previous years this method of exploring the chest for fluid, or of substantiating the diagnosis of effusion, had reserved for itself a paramount place. In spite of the fact that certain dangers attend its use, aspiration is of such value as to make one disregard them; and, to be sure, these occur very rarely, especially those which lead to untoward results. The most unfortunate of the latter is the occurrence of sudden death. The explanation of these reflex phenomena is most obscure.

As the cases present themselves it is found that the needle is most successful with the larger empyemata, especially those in which more or less total collapse of the lung has occurred. The procedure is, however, most valuable in the cases of localized collections of pus, since the physical signs are frequently inconclusive, both as to the presence and topography of the abscess cavity, while the clinical course strongly suggests the presence of a pus focus within the thorax. This is particularly so in the localized empyemata restricted to the upper areas of the chest, both in front and in the axilla, or in those confined within the borders of the pulmonary fissures. Particularly baffling are those within the axilla: it frequently happens that aspiration is practised in the usual areas, posteriorly, corresponding to the midscapular line, and in several different interspaces with negative results, while a little farther outward, toward or within, the axillary confines, purulent fluid would be produced. In actual practice it is always advisable to insert the needle in the very center of the area thought to contain fluid; toward the outer borders of the latter the layer of fluid may be thin and the needle is very apt to penetrate entirely through the fluid-containing space and to project beyond into the lung parenchyma, of course with negative results. One is frequently chagrined when, after having a great deal of difficulty in locating the pus with the needle, and after finally locating what is seemingly a small collection at some unusual and not easily accessible point, one discovers at operation that the empyema is of very large proportions thoroughly ample to cover and include every one of the aspiration areas. The reason for this difficulty is obvious from the foregoing statement.

A number of other sources of error are present in the practice of aspiration. In a number of the cases several loculi of fluid are present in the chest, and while one or several of these contain purulent exudate, another or others contain serous-like fluid (mantellergüsse of König); whenever pus is strongly suspected and clear fluid is withdrawn it is advisable to repeat the procedure at a different point in order to make absolutely sure that this snare is avoided.

In other cases the source of error lies in the withdrawal of pus when no empyema exists. On a number of occasions on the medical side of the hospital, and especially in children, the stage of resolution of a pneumonia was accompanied with symptoms resembling very

strongly those associated with purulent foci; aspiration having been practised purulent fluid was withdrawn. When transferred to the surgical side for operation the use of the needle failed to substantiate the presence of fluid of any kind* and further observation was followed by complete defervescence and spontaneous cure. It is quite likely that in these cases the needle entered a large bronchus and withdrew some of the bronchial secretion, or possibly some of the liquefied pulmonary exudate was sucked up into the syringe.

Very difficult of distinction are the purulent collections in intimate relation with the diaphragm, and with the needle alone it is frequently very difficult, if not impossible, to decide definitely whether the pus is situated in the pleural cavity or in the subdiaphragmatic space.

Roentgen Ray. Much more accurate work can, however, be done with the roentgen ray. The diagnosis of fluid can be accurately made in the largest percentage of the cases examined. In those with collapse of the lung the roentgenographic shadow is usually diffuse and covers either the entire side of the chest or its lower half or two-thirds; in these the advantage of the roentgen ray over the exploring needle is not so obvious as in those about to be described, inasmuch as it is extremely improbable for one to miss the fluid in aspirating. The superiority of the roentgen ray over the exploring needle is, however, pronounced in all cases of localized empyemata whether the cavity be relatively small and obscurely placed or whether it be limited to one of the aspects of the thoracic wall. In the former the feasibility of reaching the cavity with the needle is at a minimum and very often it is merely a matter of luck whether one succeeds in entering the cavity at all; the roentgen ray, however, gives an accurate picture of the size, the location and the relative anatomic relationships of the pus cavity, and reaching the latter with needle or incision is then a matter of comparative ease and of almost mathematical precision; stereoscopic plates are invaluable and very essential for this purpose. In the larger localized empyemata the same advantages are still present though not to such an extreme degree; much useless aspiration is, however, avoided. The manifest superiority of the roentgen ray is illustrated in the notes of the following case:

A young man had gone through a severe lobar pneumonia, and having passed the critical stage was apparently on the road to complete recovery. Fever, however, recurred and with a progressive deterioration in the general condition, a continuing loss of weight and a persistent cough, it was strongly suspected that pus was present somewhere in the chest. Repeated aspirations were negative until finally the pus was located in the axillary space by the medical consultant. A roentgen-ray picture had been taken but

* In a case of this kind the roentgen ray would be of tremendous help.

had not been properly interpreted. When I came to operate upon the patient I was able to point out the location and boundaries of the empyema cavity in the roentgenogram and to show that with proper interpretation the pus could have been reached on the first aspiration.*

The delimitation of the empyema cavity by roentgenographic study has been of particular help in establishing beforehand the most advantageous point for drainage; the site of the incision can then be accurately planned. The notes of the following case are instructive:

A boy, aged eighteen years, had been operated upon for a post-pneumonic empyema. There had been a great deal of trouble in finding the pus with the needle, but, finally, it had been located in the lower part of the right chest very far forward. The incision, which was made, corresponded to about the level of the sixth rib and was entirely in front of the anterior axillary line. Operation was, however, followed by a continuance of the fever. When I came to see the patient I was shown the roentgenograms and, even before examining the patient, I was able to point out clearly the entire boundary of the empyema cavity, to show that the pus had been reached at the most anterior and inferior part of its extent and that the entire cavity lay behind the line of incision. As the patient lay on his back in bed the drainage opening was at the topmost extremity of the cavity; retention was, of course, present, accounted for the persistence of the fever, and necessitated a second incision posteriorly, the planning of which could be accurately done before operation from the roentgenographic pictures. All of this could have been avoided by correct reading of the plates originally.*

The use of the roentgen ray affords another advantage in that frequently other unsuspected lesions are demonstrated in the picture. Perhaps the most important of these are the presence of associated pneumonic foci in the same or opposite lung. The question of whether a general anesthetic can be safely employed or whether one must have recourse to local anesthesia can then be decided much more easily and on definite criteria. The physical signs of such "silent" patches are indefinite and inconclusive and are not prominent enough to attract one's attention while examining the chest; frequently these small patches give no physical signs at all; they are, however, usually easily demonstrable in the roentgenographic pictures. A similar observation was made by Whipple several years ago; writing from the Presbyterian Hospital he pointed out how commonly postoperative pneumonias would go unrecognized because of the absence of any conclusive physical signs, if it were not for the roentgen-ray evidence. In my earlier experiences I remember

* Private records.

several occasions when the thoracotomy was very promptly followed by an exacerbation of symptoms manifestly due to an area of pulmonary consolidation; undoubtedly this had found its origin in an unrecognized, silent and perhaps defervescing patch which had been stirred up into renewed activity or had been effectually spread by the irritating anesthesia.

In exceptional cases the etiology of an unexplained empyema is clarified by the roentgen-ray studies. A very interesting case is the following:

In a man of fifty years the predominating symptoms were a continued fever and a productive cough. Repeated exploratory aspirations of the chest were negative until finally some clear fluid was withdrawn; later a thoracotomy was done. An abscess was reached presumably in the midst of the lung and drainage was instituted; the discharge from the wound resembled the purulent sputum. Drainage continued unchanged for months. Roentgenographic pictures were repeatedly made, but had not succeeded in clearing up the underlying condition. Finally in one plate a gap was noted in the dorsal part of the third rib near its bend and angle which the radiographer interpreted as a new growth. Subsequent plates showed the defect to be increasing in size. The interpretation of the clinical picture was now easily made; the man had a tumor of the lung; this had involved the pleura, induced an effusion and the latter had become infected; the rib was the site of a metastatic growth or had become involved by direct extension of the tumor.*

Treatment. The treatment of empyema is not difficult in theory but extremely difficult in practise. It involves principles established for many years. Necessarily it divides itself into that before operation, during operation and after operation.

Every empyema that one sees has gone through a stage in which the exudate was a relatively clear fluid, which, as time goes on, shows a progressive turbidity and passes finally into the stage in which the exudate is frankly purulent. As a general rule the fluid is heavily charged with bacteria and the abundance of the latter varies inversely with the length of time since the onset of the effusion; the longer the fluid remains in the chest the greater tendency there is for the bacteria either to disappear or to lose in virulence.

During the recent epidemic it rapidly became apparent that whenever the cases were operated upon very early—and this usually meant as soon as fluid accumulated in the chest—an appalling mortality resulted. Later it was learned that a policy of abstention from operation in the early periods of the pleural effusions was followed by vastly better results and that the proper time for operation only came later when the exudate was distinctly purulent, when the initial toxemia had abated or had been overcome, and

* I am indebted to Dr. Elsberg for these notes.

perhaps when the original pneumonia had disappeared. All of these facts are not peculiar to the epidemic; they are equally true of the ordinary cases. In the communication made in 1915 this condition of affairs was dwelt upon and it was pointed out how the mortality seemingly became lower and lower the longer the pus was retained in the chest. The ambiguity of the situation was also pointed out at that time, inasmuch as notoriously bad results are obtained whenever the condition is neglected and the purulent collection is undisturbed for extraordinary lengths of time; the moment for operation comes only some time after the appearance of the intrapleural process and permits of no excessive delay; the timeliness of the surgical interference is easily apparent to the clinician. A similar observation had been previously noted by Werner and the superiority of comparatively late over early operation has also received the confirmation of the Empyema Commission.

It is not definitely settled just why the initial period of a suppurative pleurisy should carry with it agencies which contribute an excessive danger to an open drainage of the chest. A number of factors seem to be present: (1) The dangers of an open pneumothorax associated, perhaps, with the spread of the infectious process to other uninvolved portions of the pleura; (2) the risks of a further compromise of lung tissue leading to a dissipation of the respiratory function until the normal reserve is exhausted to the danger-point; (3) the absence of adhesions and the failure to fixate adequately the mediastinum so that "flapping" takes place; (4) the excessive toxicity of the exudate, the increased facility afforded by operation for absorption and the inadequate preparation of the human organism in the matter of necessary antibodies to overcome the toxemia; (5) the presence of the primary illness, especially a pneumonia, still in an active state; (6) and, lastly, and perhaps most important, and perhaps the only reason, the added insult of any-operative procedure—especially one resulting in an open pneumothorax—with its unavoidable shock to a patient whose resistance, because of all things considered, is at an extremely low, if not at the lowest, level. In any individual case the correlation of all of these factors working at the same time, or the operation of any one, or any group, of them is not only possible, but extremely probable if surgical interference is undertaken at an inopportune time.

During the epidemic these facts were emphasized much more strongly than would ordinarily be possible. Preliminary aspiration of the chest as a therapeutic measure has therefore grown in favor, and it has been found advisable to repeat the evacuation of the fluid as often as the general and local signs of the patient make the indication. The chest is best emptied with some form of suction apparatus—a Potain apparatus is excellent—and as much fluid as is possible should be withdrawn; a large caliber needle facilitates

matters very much. The evacuation of the fluid is usually promptly followed by an improvement in the pulse and general appearance of the patient. Within a few hours there is an appreciable drop in temperature; in many the normal level is reached. As the fluid reaccumulates the temperature rises again; sometimes the interval between aspirations may extend to several days. A recrudescence of fever is a very good guide for the repetition of the procedure.

Repeated aspirations are usually followed by rapid improvement in the general condition of the patient. This may cause difficulty in giving the patient an unwarranted sense of cure from the purely temporizing measure; in several patients operation was, therefore, refused at the proper moment, and permission to do so was only obtained at a comparatively late interval, when the initial benefits derived from the aspirations were replaced by other disadvantages, due to the extraordinary time the pus was allowed to remain in the chest; in one of these patients return to the hospital and operation was only acceded to after the empyema had perforated through the chest wall. It is well, therefore, to explain primarily to the patient, or to the latter's family, that the aspiration is only a temporary measure and that operation is being postponed for the sake of the added safety which the temporizing measure affords.

Preliminary aspiration has been found very satisfactory for tiding the patient over the dangerous intervals until the establishment of an open drainage of the chest is fairly safe. The criteria for determining the latter point are rather crude and include the physical appearances of the exudate; the general objective signs—temperature, pulse, etc.—pointing to a diminution of the initial toxemia; and improvement in the physical signs indicating, as far as one can tell, an appreciable resolution or disappearance of the pneumonia when the latter is the primary illness. Operation should not be done until the fluid is very purulent and until the toxemia has completely disappeared.

Very rarely repeated aspirations result in a disappearance of the exudative process and an actual cure. In my own experience this has occurred only in very young children and infants. In actual practice such a small assurance of permanent cure is offered by this method as to make the possibility negligible.

The question of whether or not infection can be spread during operation to healthy portions of the pleura is very important from the surgical point of view. As one sees the cases of empyema in the hospital they fall readily into one of a number of groups.

1. The empyema is a localized abscess and, compared with the total size of the interior of one side of the thorax, is relatively small. The abscess is well walled off, the adhesions are fairly strong and manipulations must be accompanied with the exhibition of considerable force before these will rupture. If the condition has existed for a considerable length of time—several weeks—the adhe-

sions are very firm indeed, much firmer than any adhesion ever seen in the abdominal cavity, and even at postmortem examinations it is next to impossible to tear these apart; almost always the pulmonary parenchyma ruptures before the scar tissue in the pleura gives way.

2. In the second group the lobes of the lung on the affected side have collapsed and have become fixed in place in a more or less shrivelled state in the interval formed by the curvature of the ribs and close to the spinal column. The degree to which the lungs have collapsed may be extreme or may be at a minimum; in the former the thoracic cage is practically in its entirety an abscess cavity; in the latter the cavity is rather shallow, although it extends from the upper to the lower limits of the thorax and is most frequently in relation with the axillary portion of the chest wall. In between these two extremes all grades can occur. In the extreme cases practically the entire extent of the pleura, both visceral and parietal, is compromised in the infectious process and no further extension can conceivably take place. In the others the differentiation from the cases in the first group is one only of relative size. Here, too, the character of the adhesions present is exactly similar, and, while when the condition is still fresh they may give fairly readily to the finger, as time goes on, they acquire more and more a cartilaginous consistence and the use of scissors and scalpel are required before the parts can be separated.

On a number of occasions while operating upon children and when conditions similar to those described were present, I have purposely broken through the limiting adhesions bluntly with the finger and have liberated the lobes of the lung as far as I could reach. It was easy in the children to reach as high as the apices of the upper lobes and widely from side to side. Comparatively large areas of uninfected and uninvolved portions of the parietal and visceral pleura were bared to the infection; yet the clinical course after operation gave no indication either in temperature, pulse or other objective or subjective symptom that the pathological process had been increased in extent.

3. The third group includes the cases of empyema associated with lung abscess for which radical operations (lobectomy) are done. Under such conditions the actual proof of the spread of intrapleural infection during operation has been given to me on one occasion, but I do not believe this experience to be unique.

This was a man with a pulmonary abscess fairly well localized in the upper right lobe. A lobectomy was done while the rest of the pleura was guarded from infection by appropriate means. At the conclusion of the operation the resultant cavity was lightly packed with iodoform gauze; in addition a counteropening was made into the costophrenic sinus and a tube was led in through this opening and brought up to the level of the uppermost portion of the

thorax near to the stump of the upper lobe. The man died some ten days later. The postmortem examination showed marked infection of the cavity resulting from the extirpation and an abscess between the under surface of the lower lobe and the upper surface of the diaphragm which did not communicate with the drainage tract. The intervening portions of the thorax were apparently clear, though, to be sure, the visceral and parietal pleuræ were adherent throughout with the exception of that part occupied by the tube (drainage tract).*

Cases of this kind are really primary operative infections of the pleural cavity and resemble very much infection of the peritoneum during a laparotomy with residual abscess formation.

The assumption seems justifiable, therefore, that in the ordinary case of empyema the danger of spreading the infectious process by open thoracotomy is relatively small. In truth the present custom of operating does not permit of any spread of infection. The extent and boundaries of the empyema cavity are accurately delimited prior to operation by adequate roentgen-ray examinations, so that the most favorable point for drainage can be definitely established beforehand. The operation, and this, of course, refers to the early cases and to primary operations carried out at the most opportune time, becomes then merely an incision into an abscess (empyema) cavity and the institution of proper drainage; such a procedure carries a minimum of danger of spreading the infection. In the very exceptional case in which for one or another reason it is deemed advisable at the primary operation to part the adhesions in order to liberate the lobes of the lung, the experience detailed seems to show that little need be feared of the danger of spreading the infectious process to hitherto uninvolved surfaces in all but the lung abscess cases.

Perhaps in some of the cases which have come under my observation some spread of infection has occurred, but having given no perceptible evidence it was unrecognizable in the general clinical picture with the means at our command. Such an occurrence is wholly compatible with the statement made immediately preceding. The character of the infecting organism and the intensity of its virulence as compared with the resisting powers of the patient would have most important bearings on this phase. In several children, in whom the presence of no adhesions and the involvement of the total parietal and visceral surfaces of the pleura indicated that the process most probably followed the rupture of a small superficial focus of liquefaction in a pneumonic lobe, (Rosenbach) a thorough consideration of the history and the clinical course failed to show that any extraordinary symptom had marked the onset of the pleuritis

* Case from surgical service, Mt. Sinai Hospital.

and its conversion into an empyema. On the other hand the phenomena accompanying the rupture of an acute pulmonary abscess into the pleural space is marked by an extreme increase in the clinical symptoms, and especially in the toxemia. The manifestations of an operative infection of the pleura, as, for instance, that following a lobectomy for a chronic lung abscess, are not so prominent and are probably much mitigated by the immediate institution of ample drainage.

Methods of drainage of the chest, now as formerly, are essentially one of two—intercostal incision* and rib resection. Intercostal incision is the older operation. Many years ago it was the operation universally employed; but there was much difficulty with the after-treatment, especially from the point of view of securing adequate drainage, and gradually the method was abandoned and replaced by rib resection. In the series which I studied and reported in 1915, 21 of the patients (total number 299) were operated upon by intercostal incision. These were the desperately sick cases, and the operation was done as a matter of expediency rather than as a matter of choice. The important point that was brought out was that there never was any trouble in securing adequate drainage; the healing of the wounds was not only not impeded but actually hastened. Since that time my experiences have only served to substantiate this viewpoint, and I have done intercostal incision practically to the exclusion of other methods. At the present time there seems to be little doubt that from the mechanical point of view intercostal incision and rib resection are equal for drainage purposes, and if intercostal incision is otherwise satisfactory for desperately sick patients, I can see no reason why it should not be equally efficient for the ordinary cases. I have had no cause to regret this attitude, and since the outbreak of the first epidemic of influenza and since the occurrence of the large numbers of pneumonias, with their consequent empyemata, in the various army camps, this opinion seems to be confirmed by the increased favor with which intercostal incision is being regarded throughout the country.

It is difficult to understand why the opinion should have become prevalent that intercostal incision does not yield a drainage equal to that obtained by rib resection. By using one or several appropriately sized tubes and making the incision between the ribs long enough a comparatively large opening is very readily obtained both in children and in adults. As a matter of fact the actual opening

* Continuous drainage through an intercostal opening made with an ordinary trocar is after all nothing but an intercostal incision. In children and infants it may be all that is needed; in adults the opening obtained is much too small for efficient work especially when one wishes to make use of irrigations with an antiseptic solution. When combined with suction it is, of course, the old Bulau method of treating empyema.

leading into the thorax, when rib resection is done, is very seldom any larger than that obtained with intercostal incision; it is only the outer wound, perhaps, which is larger and that is inconsequential. When the tube, or tubes, are properly placed there are no impedimenta to the outflow of the thoracic contents; drainage is perfect and no retention of pus can be demonstrated. I have frequently seen retention and fever after thoracotomy for empyema, but just as often this was present in cases which had had a rib resection done as in those with intercostal incisions, and I feel quite sure that many other men have had similar experiences.

Except for some special purpose I have abandoned rib resection, and as time goes on the exceptions to the rule and the special reasons are growing less. There are two very valid objections to rib resection as I see the problem since an equally efficient drainage can be accomplished with intercostal incision.

The usual method of doing rib resection is practically an enucleation of a segment of rib from its periosteal covering. When done in that way much newly formed bone is thrown out from the osteogenetic layers, and because the latter lies on the inner side and circumscribes the drainage tract the new bone is crowded in between the adjoining ribs; commonly it becomes superabundant; large plates of bone then form which cause mechanical hindrances to the normal respiratory excursions of the chest wall. The sinus itself becomes surrounded by a bony wall which, more frequently than is apparently recognized, forms an obstacle to the proper closure of the sinus. Both of these form prolific sources for the formation of chronic empyema sinuses and for repeated operations. Both of these undesirable phases can be obviated by excising the rib *in toto* after the suggestion of Lilienthal.

A solution of continuity of the rib opens up surfaces of bone tissue to infecting agencies. In the previous communication (1915) I was under the impression that this was immaterial and that the rib was able to avoid, or quickly overcome, any infectious process to which the environment might lay it open. I have since been disillusioned. Fairly frequently the rib becomes infected, an osteomyelitis affects the rib for a variable distance from the cut surface and healing is prolonged until the dead bone is cast off or until a similar result is obtained by operation. The process may also involve any part of the new bone formation which is thrown out around the drainage tract. When the segment removed is in the immediate neighborhood of the costal cartilages the probabilities are strong that the cartilage, too, will become infected; this would be a rather serious complication. In a communication relating to the infections of the cartilages, Moschcowitz[7] pointed out that an infected cartilage never heals spontaneously, and only heals after operation when every bit of it is removed down to healthy portions of the bone to

which the cartilage is attached. In the connecting segments of the cartilages this would entail an extensive secondary operation before closure of the sinus results.

All of these troubles can be very nearly avoided by making the intercostal incision. Occasionally when a tube too large for the intercostal space is employed, pressure necrosis of the soft parts overlying the rib results in a superficial baring of the bone; the latter does not compare, however, with the osteomyelitic process set up in a resected rib.

A very important advantage of intercostal incision is that the operation can be very easily done in bed. With a very sick and toxic patient, or in one with a badly compromised circulation, the transportation of the patient to and from the operating room is a very serious item. I am quite sure that several of the fatalities which I have seen have been due to this cause. The simplicity of intercostal incision, as compared with rib resection, is extreme.

I believe that it is important not to make the drainage opening in the chest wall of larger caliber than the diameter of the main bronchus entering the lung. Expansion of the lung is a very necessary factor in the contraction of the empyema cavity, and it is only accomplished by the current of air entering and distending the interior of the lung. Ordinarily this has no opposing force. With a fistula in the thoracic wall a current of air is sucked into the empyema cavity with each inspiration, and if its volume is larger than that entering the normal channel, no distention of the lung substance occurs.

The simplest form of drainage apparatus—an ordinary rubber tube—is the best. It is usually taught that it is sufficient for the tube to project just within the inner surface of the thoracic wall in order to obtain complete drainage. Theoretically this should be so; practically it is very frequently not so, especially with the larger cavities, and drainage is not efficient. It is found to be better practice to allow the tube to project into the thorax for a little way and to shorten it progressively as the empyema cavity shows signs of contracting. Various forms of drainage apparatus, with and without valve formations, and manufactured of various materials, have been proposed and employed, and each is said to have some special advantage; but none of these can compete in flexibility of application with the ordinary rubber tube.

In the last two or three years the addition of a suction apparatus in the after-treatment for the purpose of aiding the constant evacuation of the chest has become very popular. The method is a very valuable adjunct to the treatment of empyema. It is most comfortable for the patient; it eliminates many dressings; it reduces the bulk of the dressings to be carried; it permits the collection of the wound discharges in some kind of receptacle and prevents the

maceration of the skin; the pressure in the empyema cavity is more easily kept at a lower level than that in the bronchi and in the interior of the lung and because of this the expiratory effort can more easily help in the contraction and obliteration of the empyema cavity. A disadvantage of the method is that with all the various means of applying suction the patient must necessarily be confined to bed as long as the suction is maintained. A doubtful amount of suction can be maintained by means of a Politzer bag, as in the method described by Bryant. I believe, however, that the method is not very efficient, and after the first few minutes of its application the bag probably exercises none of the function for which it was intended; it is necessary to have the sucking device constantly active to overcome the leakage which occurs around the drainage apparatus.

The antiseptic treatment of empyema wounds has grown very much in favor. The principles and technic, as developed by Carrel and Dakin, are employed for this purpose. It is hoped to secure a complete sterilization of the empyema cavity with the object of secondarily closing the outer wound; the length of time necessary for complete cicatrization of the wound is thus very materially shortened. In actual practice this ideal result is not always accomplished because of the following reasons: in empyema complicated by broncho-pulmonary-cutaneous fistula the method is not applicable; it is very frequently impossible to secure complete sterilization, owing to the difficulties of the technic to be employed; when, apparently, sterilization is secured, closure of the outer wound by suture is not always successful, or a secondary collection of pus having accumulated within the thorax the wound reopens shortly and the entire curriculum must be gone through again.

The difficulties in securing complete sterilization are the real obstacles to the successful employment of an otherwise very valuable method. There are a number of reasons why it is frequently impossible to sterilize the cavity: (1) Very often there are sacculations to the cavity connecting with one another by comparatively small and not easily accessible channels; or there are several independent collections of pus situated at different locations within the thorax; if the antiseptic solution does not reach every part of the interior of the cavity the method is, of course, futile. (2) Small foci of infection can be located in one or many parts of the wall of the empyema cavity, and when liquefaction occurs the pus ruptures into the empyema cavity and reinfects the latter. These foci may be in the superficial parts of the pulmonary parenchyma and result from the original pneumonic condition, or they are in the parietes. The most important of the latter reside in the ends of the resected ribs: I referred above to the disadvantage of rib resection; the parts involved in the osteomyelitic process form a nidus from which the

constant reinfection of the empyema cavity takes place. (3) At any portion of the wall of the cavity the progressive contraction of the latter often lends itself easily, from the formation of superfluous adhesions, to the production of small retention abscesses; sooner or later these rupture and reinfect the original cavity. All of these may lie dormant for relatively long periods of time and I believe that at least some of the "secondary empyemas" which make their appearance after the thoracotomy has apparently healed solidly are due to such causes.

In the instillation of Dakin's solution into the empyema cavity there are wide differences in practice among all of the men especially as to the amount of fluid to be employed. Some use a comparatively small amount—10 to 15 c.c.—others use relatively larger amounts; many use an arbitrarily chosen quantity—usually about 100 c.c.—or the quantity is determined by the length of time the fluid is allowed to run into the chest. Such practice is characterized by a certain timidity and lacks the precision which is a highly desirable factor. Inasmuch as it is very essential to secure an actual contact between antiseptic solution and the entire surface extent of the cavity to be sterilized in order to secure the actual sterilization, it is necessary in some way to employ the method with this object in view. Many employ a number of Carrel instillation tubes, which, being stiffened with wire, are made to reach all surfaces of the cavity; the fluid flowing inward is thus made to reach all surfaces; the amount of solution is, however, comparatively small; the contact of fluid and wall is only present for a few seconds, and thereafter the fluid settles in the bottom of the cavity and a relatively large part of the interior is not in contact with the solution.

I make use of a large tube for drainage, which is coupled with the suction apparatus. The tube leading from the chest to the collecting bottle is made to connect by a T-tube with the reservoir containing the Dakin solution. The total capacity of the empyema cavity is measured with water and noted. The amount of Dakin's solution which is instilled at two-hourly intervals is equal to a few cubic centimeters less than the measured capacity. At the appropriate time the suction is blocked off with a clamp and the Dakin solution is allowed to run in to the amount indicated. Inasmuch as the effect of the free chlorin liberated from the solution is only operative for a very few minutes, there is no necessity for allowing the solution to remain in the chest for any length of time and at the end of fifteen minutes the suction is reëstablished and the entire contents are evacuated from the thorax. The suction is allowed to continue until the next instillation. If desirable the procedure can be repeated at hourly, instead of two-hourly, intervals.

It seems to me that this method is most satisfactory for assuring an intimate contact of antiseptic solution and surface to be sterilized.

The large amount of fluid, employed as I have indicated, flows easily into the main cavity; it flows just as easily through any narrow communication into any subsidiary loculi or around any obstructing adhesions; it makes contact efficiently with smooth or distorted or irregular cavity walls and with that of any subsidiary cavities; it remains in contact for the full time for which the fluid is of any use.

The use of any method of irrigation is a new departure from the custom maintained up to the time of publication of the studies of Carrel and Dakin. One has always been taught that irrigation of any kind is dangerous when employed within the chest and from time to time serious consequences have been reported. The knowledge has, perhaps, been a deterrent to the use of Dakin's solution in some quarters and has encouraged the use of small quantities cautiously instilled in others. It is known that similar accidents follow the use of other intrathoracic procedures, especially puncture and aspiration of the chest. There have been no untoward effects or results in my experience with Dakin's solution. I realize, however, that a certain amount of danger exists, but I believe that the method ought to be persisted in because of its intrinsic value, especially since the actual danger of the irrigations is after all relatively and numerically very small.

The presence of a bronchopulmonary fistula of any magnitude makes the method impossible of application, owing to the "gassing" of the patient by the liberated chlorin gas. I remember several patients who showed a moderate amount of distress from this irritation, and if I had followed the usual practice I should have immediately abandoned the irrigations as part of the after-treatment. On subsequently repeating the irrigation I was surprised to note the absence of any irritative signs and thereafter the solution was tolerated very well. I remember in a number of other patients that signs of chlorin irritation were apparent at late periods of the postoperative course which were present on only one, or at most several, occasions in each patient, but which were not sufficient to deter us from continuing the use of Dakin's solution. The probabilities are that minute fistulæ were present which in some way were quickly closed, or which, because of their tortuosity or other mechanical obstruction, did not always permit any of the solution to enter the parenchyma of the lung. Perhaps the irritation of the chlorin was itself effective in closing the fistulæ because of the inflammatory swelling of the tissues making the sinus tract. At any rate if the initial trial of solution is followed by embarrassment the effect ought to be corroborated by a second more carefully carried out instillation before the irrigations are definitely abandoned.

There is a great deal of difficulty in making an accurate determination of the sterility of the cavity. The smear method is not at all reliable, not only because of the possibilities of error while looking

through the smear, but because it is common knowledge that many colonies of bacteria will grow on media when no organisms are visible in the smear. Cultures are always necessary. The sterility of the outer wound is quite easily demonstrated; within the cavity it is not possible to reach all parts for specimens; and while seemingly all that are obtained are sterile, other foci may be present which harbor many organisms. It is quite true that an absolute sterility is not necessary for the secondary closure of the wound.

As soon as the sterility of the cavity is established with a reasonable degree of certainty the practice is to discontinue all forms of irrigation or other treatment. The immediate suture of the outer wound is perhaps not advisable, owing to the frequency with which the wound reopens to permit the discharge of retained pus. It is much better practice instead to simply cover the wound with a dry dressing and to permit the wound to heal by granulation. The outer wound closes very rapidly; a larger or smaller cavity—a pneumothorax—remains which, when truly sterile, does no harm; after a time the pneumothorax becomes absorbed and the cavity becomes obliterated. The pneumothorax shows no clinical evidences either subjectively or objectively. Permanent healing of the cavity must necessarily occur by complete obliteration. This probably occurs as a creeping adhesion of the adjoining parietal and visceral edge of the lining granulation membrane.

In order to obtain good results constant and persevering attention is needed in the postoperative period. The work of the Empyema Commission has shown the importance of maintaining the nourishment of empyema patients at as high a level as possible; special attention is necessary to the nitrogenous elements of the diet. This corresponds with our previous knowledge in regard to the feeding of patients afflicted with suppurating foci. The importance of not neglecting the primary condition to which the empyema is secondary cannot be overemphasized and the rule holds good both with the epidemic and with the ordinary cases. During the postoperative course the primary illness—especially the pneumonia—may continue, or, after it has apparently subsided, it may recrudesce. Other complications are numerous and in children these frequently take the form of intercurrent disease having no or little relation to the thoracic condition. The importance of all of this is readily appreciated when it is known that under ordinary circumstances approximately 20 per cent. of empyema patients die as a result of the primary illness, or of a recurrence of it, or of some other complication or intercurrent disease; under extraordinary conditions (epidemics) the percentage is considerably higher. The table of complications given in my 1915 communication is reproduced for the sake of emphasis.

TABLE OF COMPLICATIONS.

	Cases.	Deaths.
Pneumonia	23	19
Pneumonia and pleural effusion	2	2
Bronchial fistula	4	
Empyema on other side	2	2
Pulmonary edema	4	4
Bronchiectasis	1	
Cellulitis of chest wall	2	
Necrosis of resected rib	4	
Subcutaneous abscess at a distance from the empyema wound	9	
Brain abscess	2	2
Bacteremia	5	5
Tuberculosis of the resected rib	1	
Middle ear suppuration	14	2
Thrombosis of lateral sinus	1	1
Meningism	2	1
Cerebrospinal meningitis	1	1
Tuberculous meningitis	1	1
Acute endocarditis	1	1
Myocarditis	1	
Acute insufficiency in chronic valvular disease of the heart	1	1
Nephritis	4	2
Nephritis, pulmonary edema	1	1
Pyelitis	1	
Catheter infection in a tabetic	1	1
Pharyngeal diphtheria	1	
Measles	2	
Pertussis	1	
Scarlet fever	1	
Enterocolitis	2	2
Follicular tonsillitis	1	
Rickets	1	1
Marasmus	2	2
Subacromial bursitis	1	
Pott's disease of the spine	1	
Amyloid disease of the viscera	1	
Nevus of vocal chord; asphyxia	1	1
Acute mastoiditis	1	

The important complications listed by Stone,[7] Bliss,[5] and Phillips[9] (Fort Riley cases) include the following:

Pericarditis	5.9 per cent.
Large pleural effusion	4.8 "
Substernal pus pockets	3.3 "
Pulmonary abscess	3.0 "
Peritonitis	2.7 "
Endocarditis	1.2 "
Miliary tuberculosis	0.8 "
Meningitis	0.3 "
Pulmonary embolism	0.2 "

The important complications listed by Vaughan and Schnabel[10] (Camp Sevier cases) include pericarditis, urticaria, peritonitis and arthritis. Multiple complications were common. The complications noted by Stone, Bliss and Phillips[9] and by Vaughan and Schnabel[10] reflect more especially conditions associated with epidemic conditions.

In the postoperative period fever of one kind or another is a very common phenomenon. Most frequently it is due to any one, or more, of the complicating conditions just enumerated and the explanation of the fever is simple; occasionally the demonstration of the cause is difficult. Very commonly fever is due to the retention of pus within the wound; very commonly the amount of retained pus does not correspond, apparently, with the degree of fever but improvement in the drainage immediately results in the fall of the temperature. The retention of pus is sometimes located within the pulmonary parenchyma either in a definite focus of lung suppuration or within the confines of a bronchopulmonary fistula, from either one of which the escape of the purulent discharge is temporarily impeded.

A moderate grade of fever running along for some time is quite commonly caused by an osteomyelitis of the rib.

Under the newer methods of treatment there has been a pronounced improvement in the results obtained with operations for empyema. Less frequently than heretofore the sinus in the chest fails to close within a reasonable length of time. Difficulties arise with the interpretation of the latter term, for a length of time which is "unreasonable" to one man is regarded with more or less indifference by another. Lilienthal[14] waits only a very short time after doing the primary intercostal incision—minor thoracotomy—before he proceeds to do his larger operation of major thoracotomy; he believes the secondary procedure necessary in a great many of the cases. Recently, Aschner, who is associated with Lilienthal, expressed the opinion* that the secondary major thoracotomy is not necessary as often as was first believed. My own experience has led me to the opinion that minor thoracotomy is all that is necessary in the very great majority of the patients when none of the impeding factors spoken of below are present. In any case I am accustomed to wait a very long time before doing any secondary operation as long as I am sure that drainage is perfect and that there are no mechanical factors interfering with the cicatrization of the wound. I was very much influenced toward this opinion by the course of the healing of the wound in the following case:

A middle-aged man was operated upon by rib resection for a postpneumonic empyema; the sinus persisted for fifteen months, at the end of which time I saw the man for the first time. A small opening was present in the chest which discharged some foul pus; the roentgen ray showed a homogeneous shadow covering the whole of the involved side. A radical operation having been determined upon the chest was opened widely through an intercostal space and the incision was prolonged upward, posteriorly, parallel to the spine, with division of the ribs (Torek). An enormous cavity was dis-

* In a personal communication this opinion was confirmed by Lilienthal.

closed reaching from the very top to the very bottom of the thorax and fully as wide as the depth of the chest. Owing to the presence of a large amount of very foul pus the intention to proceed with an extensive thoracoplasty (Schede) was temporarily abandoned until the suppuration could be controlled. The wound was left wide open and was dressed after the Carrel-Dakin technic. At the end of six months the outer wound had contracted and closed down to a very narrow slit. I had hoped from the way the wound had been healing that any further operation would be unnecessary; but at that time six months seemed "unreasonably" long and I determined to proceed with my original intention. On reopening the wound I was astounded to see that the original huge cavity had contracted down to a narrow gutter barely a finger's breath in width. I am quite sure that if I had waited but a little while longer, the entire wound would have closed spontaneously.*

There are a number of factors which interfere with the closure of the thoracic sinus after operations for empyema. Practically all of these functionate by constantly reinfecting the cavity which is to cicatrize, and many of them are those which interfere with the proper sterilization of the wound with Dakin's solution. Over some of these we have almost perfect control, as, for example, a badly carried out drainage or an osteomyelitis of the resected rib. Over others we have only partial control: such would be those empyemata which are not simple cavities but in which the main cavity is complicated by subsidiary loculi; the drainage of the latter is at best imperfect.

The more I see of empyemata the more I am convinced that the greatest obstacle to healing is the presence of a bronchopulmonary fistula: over this impediment we have no control at all. The fistula may be so small as to readily escape demonstration. I feel convinced that bronchopulmonary fistula is a very frequent complication of empyema even in cases in which no disturbance in the healing is apparent and in which, of course, no inkling of its presence can be furnished. This should not appear extraordinary in view of the opinion that many, if not all, of the empyemata complicating pneumonia result from the superficial abscesses (Rosenbach)[13] which rupture into the pleural cavity. The importance of bronchopulmonary fistula in causing chronic sinuses seems to be corroborated by the further observation that almost all of the chronic sinuses follow the postpneumonic type of empyema. My experiences seem increasingly to show that as a cause for chronic empyema sinuses, bronchopulmonary fistula holds first place.

In previous years much has been said about rigid cavities as efficient causes for the failure of closure of the thoracic sinuses. I do not believe, however, that the rigidity of the empyema walls—and

* Private records.

here, of course, I speak especially of the visceral layer—is a primary phenomenon. I have the impression that it is distinctly a secondary process, owing its presence to any one of the causes mentioned in this communication, which functionate as impedimenta to the healing by constantly reinfecting the cavity. The constant reinfection is conducive to an overproduction of scar tissue in the granulation membrane lining the cavity, and the superabundance, by its very massiveness, lends the unyielding qualities to the visceral surface. A vicious circle is thus formed, so that frequently a pneumolysis of some sort is necessary to permit, or to aid in permitting more rapidly, the expansion of the lung. But in very many cases the efficient removal, operative or otherwise, of the essential primary cause is followed by a progressive yielding of the membrane and an obliteration of the cavity. It is significant that with increased knowledge much less has been said in the last few years of rigid cavities as causes for chronic empyema sinuses.

Recurrences of empyema are fairly common. I should rather term this an incomplete healing of the original empyema. The essential cause for this accident is again an incomplete sterilization, or a reinfection, of the cavity; and the causes for the latter include: (1) Incomplete obliteration of the original cavity; (2) a bronchial fistula; (3) rib sequestra; (4) islands of dormant bacteria in the walls of the empyema cavity; and (5) the retention of foreign bodies.

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SUBSTERNAL GOITER, WITH PRESSURE SYMPTOMS.[1]

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Summary. Female, aged sixty-four years, suffering from goiter, with symptoms of hyperthyroidism. Enlargement of the thyroid

[1] Read by title at the meeting of the Association of American Physicians, Atlantic City, May 4 and 5, 1920.

gland above the sternum very marked. The tumor also extended below the sternum and by pressure on the right phrenic nerve produced paralysis of the right side of the diaphragm and by pressure on the recurrent laryngeal nerve produced partial paralysis of the right vocal cord; it also displaced the heart toward the right side, producing a loud systolic murmur, with its intensity at the apex and a marked myocardial insufficiency.

Treatment. Roentgen ray, rest and medication.

Result. A fairly satisfactory recovery, the paralysis of the right diaphragm and right vocal cord remaining.

April 10, 1917. *Personal History.* Thirty-three years ago the thyroid gland began to enlarge and it has been enlarged ever since, but the patient has never had any symptoms referable to this condition. In 1916 I found pus in her urine, which readily yielded to treatment with urotropin and benzoate of soda. In the winter of 1917 pus was again found in her urine and disappeared under the same treatment.

December 1. The patient's present illness began during the summer of 1917, while at her summer home at the seashore. During August of this year she suffered from mental depression and shortness of breath. Early in September she consulted a physician, who found that she had a well-marked cardiac murmur and that her urine contained pus.

About the middle of October she was taken to New York and placed under the care of a physician, where she remained until her return to Cincinnati on November 29, 1917. Her physician in New York reported that she had dyspnea on exertion, a well-marked systolic heart murmur, a blood-pressure of 148–74, a sterile blood culture and a negative Wassermann. On October 22 a blood examination showed hemoglobin 85 per cent. red blood cells 5,400,000, white blood cells 5000, polymorphonuclears 41, lymphocytes 54, eosinophiles 5. The urine examined on October 22 and November 12 contained no pus, and except for a very faint trace of albumin was negative. The patient was kept off her feet and in bed the greater part of the time she was in New York, and during this time she improved very materially. The cardiac dulness decreased.

On sending the patient to Cincinnati her physician wrote: "I feel that Mrs. Blank has for a basis of her cardiac changes a mild hyperthyroidism. She has had from time to time, in addition to the goiter, the following clinical evidence to substantiate this view: (1) Instability of pulse and a marked tendency to develop tachycardia; (2) flushing; (3) tremors."

November 30 I saw the patient at her home, twenty-four hours after her arrival from New York. She had been in bed during that time; she had symptoms of mild hyperthyroidism, a loud systolic murmur was heard most distinctly near the apex of the heart, which was transmitted into the axillary region, and was also heard very

distinctly in the direction of the sternum, extending quite far up along the sternal line over the arch of the aorta. No diastolic murmur was heard. There was a dull area beneath the manubrium continuous with the cardiac dulness; the latter was increased downward and outward.

The left lung appeared normal but the lower border of the right lung upon percussion and auscultation did not appear to extend below the 7th or 8th rib posteriorly and the 4th rib anteriorly. Vocal resonance and fremitus were diminished or absent over the lower portion of the right chest. The vesicular sounds over the whole right lung were less distinct than over the left.

December 6, Dr. Samuel Iglauer, in consultation, found the left vocal cord paralyzed, and the inference was that this paralysis was produced by pressure from some substernal growth or from an aneurysm of the aorta.

A roentgen-ray examination made at this time was as follows: The stereoscopic roentgen-ray plates of the chest showed an opaque shadow beginning just above the arch of the aorta, extending up into the neck, where it became lost in the shadows of the deeper structures. This shadow extended about two inches to both sides of the sternal line. The arch of the aorta on its curve on the left side showed a number of dense shadows simulating calcareous deposits. The lower right side of the chest was opaque. The opacity extended posteriorly from below upward as high as the 8th rib and anteriorly as high as the 4th rib. The line of this shadow was straight and was evidently the lower border of the diaphragm. The fluoroscopic examination showed the same shadow in the same position, with no apparent movement of the diaphragm on the right side. The heart shadow appeared normal in size and pushed slightly to the left.

The roentgen-ray films of the teeth showed no root abscesses.

A blood examination showed hemoglobin 85 per cent., red blood cells 5,000,000, white blood cells 5200, lymphocytes 37 per cent., large mononuclear leukocytes 7.66 per cent., polymorphonuclear neutrophiles 52.66 per cent., eosinophiles 1.3 per cent., mast cells 1 per cent., myelocytes 0.0, Tuefck's irritation forms 0.3 per cent.

At this time, in addition to the diagnosis of enlarged thyroid with hyperthyroidism, it was our belief that that portion of the enlarged thyroid gland extending beneath the sternum pressed upon the recurrent laryngeal nerve, producing paralysis of the vocal cord, and also pressed upon the right phrenic nerve, producing paralysis of the diaphragm.

This patient was seen in consultation by Dr. Roger Morris and Dr. Max Dreyfoos on December 17, and on January 26, 1918. She was also seen on January 28, 1918, by Dr. James B. Herrick, of Chicago.

The physical findings and diagnosis as above recorded were con-

firmed by the consultants, and it was decided to seek surgical advice with reference to the advisability of a surgical operation.

It was the opinion of myself and all the medical men who had studied this case that it was not advisable to attempt the removal of the substernal thyroid, which was producing the pressure symptoms.

During the last week of February, 1918, the patient was taken to Chicago for medical and surgical advice. She returned to Cincinnati in about ten days, with medical and surgical opinions that it was not advisable to attempt an operation, and also with the advice that the medical treatment which she had had before going to Chicago should be continued.

At this time the prognosis was considered very bad by all the physicians and surgeons who had seen her. On her return to Cincinnati the treatment which she had received from the time she came under my observation was continued, and the remarkable improvement in her physical condition which has resulted I think justifies the clinical report here given.

Treatment. On December 1, 1917, when the patient first came under my observation, she was given 15 drops of tincture of digitalis three times a day. From that date to the present, covering a period of two years and four months, she has continued to take digitalis, omitting it for only short periods of time. At the present time she is taking 5 drops of the tincture twice a day, six days in the week. The dose has been gradually diminished and has been omitted occasionally for short periods. During nearly all of this time she has taken a capsule containing 2½ grains of the neutral bromide of quinin, 1 grain of extract of ergot and $\frac{1}{30}$ grain of extract of belladonna.[2] This capsule was given three times a day for a long period of time, and throughout the two years and four months it has been taken almost continuously. During the past year she has taken two of these capsules per day. At rare intervals this treatment has been interrupted for a period of a few weeks.

In addition to the above treatment the patient took deep roentgen-ray treatments over the thyroid gland, given from two areas in the front and two in the back, never giving more than two areas at one time. These treatments, fifteen in all, were given by Dr. William M. Doughty on the following dates:

1918—January 4 and 15; March 5, 15 and 29; April 12 and 26; May 17; June 8; November 8; December 2.

1919—January 7; April 15; May 20; June 9.

These treatments were all filtered through 4 mm. of aluminum.

When the patient came under my observation, December 1, 1917, she was practically confined to her room, spending most of the time in bed or upon a couch. Even the slight exertion of walking about

[2] The above prescription was a favorite one of the late Dr. Frederick Forchheimer, of Cincinnati.

the room produced shortness of breath and increased rapidity of heart action. During this time she was occasionally carried up and down stairs, and some months later was strong enough to take automobile drives. After four or five months of treatment her heart had sufficiently recovered for her to walk up and down stairs once a day. She has steadily improved in strength, so that at the present time she leads practically a normal life and presents the appearance of being in perfect health.

The physical signs so far as the lungs are concerned persist. The right diaphragm is in the same position as above described. An examination of the heart still shows a systolic murmur, which is loudest at the apex. This murmur, however, is now soft and very much diminished in intensity, and in the range of its transmission. It is my belief that at the present time the shortness of breath, still experienced after taking long walks, is due rather to the diminished lung capacity of the right lung than to any cardiac weakness.

The patient has not had a roentgen-ray treatment for nearly a year, and for more than a year there has not been any evidence of hyperthyroidism.

REPORT OF A CASE SHOWING THE RELATION BETWEEN OCCUPATION AND A CERTAIN CASE OF BRONCHIAL ASTHMA.

By Jacob Rosenbloom, M.D., Ph.D.,
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It will be recalled that our present conception of bronchial asthma differs greatly from that previously held. We now know that by means of the cutaneous or skin test cases of bronchial asthma that are sensitive[1] to proteins may be separated from the non-sensitive type. The first class, or true bronchial asthma, is separate and distinct from the second, non-sensitive type, the so-called asthmatic bronchitis.

The following classification of Walker[2] presents this in an interesting way:

[1] For studies showing possible relationship of bronchial asthma to anaphylaxis and to the amins see: Friedberger and Moreschi: Berl. klin. Wchnschr., 1912, xlix, 741. Oehme: Arch. Pharm., 1913, lxxii, 76. Baehr and Pick: Arch. f. exper. Path. u. Pharm., 1913, lxxiv, 41, 65. Meltzer: Jour. Am. Med. Assn., 1910, lv, 1021; Tr. Assn. Am. Phys., 1910, xxv, 66. Eustis: Am. Jour. Med. Sc., 1912, cxliii, 862; New Orleans Med. and Surg. Jour., 1914, lxvi, 730; 1909, lxi, 98. Eppinger and Gutman: Ztschr. f. klin. Med., 1913, lxviii, 411. Dale and Laidlaw: Jour. Physiol., 1910, xli, 318; 1911, xliii, 182. Pfeiffer: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1911, xi, 133. Biedl and Kraus: Ztschr. f. Immunitätforsch. u. exper. Therap., 1912, xv, 447. Schittenhelm and Weichard: München. med. Wchnschr., 1912, lix, 67. Aronson: Berl. klin. Wchnschr., 1912, xlix, 642.

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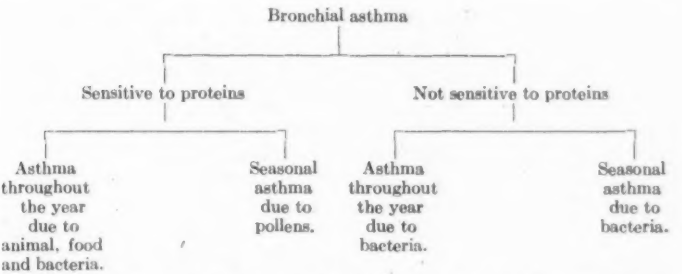
Bronchial asthma
Sensitive to proteins
Not sensitive to proteins
Asthma throughout the year due to animal, food and bacteria.
Seasonal asthma due to pollens.
Asthma throughout the year due to bacteria.
Seasonal asthma due to bacteria.

The following are the essential points, in the history of the case of true or sensitive bronchial asthma, that I wish to report.

Mr. Z., aged forty-four years, a baker for twenty-six years, has suffered continually from chronic bronchial asthma for a period of fourteen years. About every second or fourth week he develops an acute attack. The physical examination shows some emphysema, otherwise it is negative. Laboratory examination of the urine, blood and feces reveal nothing of importance.

The patient was tested with the following proteins:

Almond	Egg, whole	Perch
Asparagus	Egg yolk	Pike
Banana	Fig	Pineapple
Barley	Ginger	Plum
Bean	Goat meat	Pork
Beef	Goose	Potato
Beet	Grapefruit	Radish
Blackberry	Guinea-hen	Raspberry
Bluefish	Haddock	Rhubarb
Brazil nut	Herring	Rice
Buckwheat	Lactalbumin	Rye
Cabbage	Lamb	Salmon
Cantaloupe	Lentil	Sole
Carrot	Lettuce	Spinach
Casein	Lima bean	Squab
Cauliflower	Lobster	Squash
Celery	Mackerel	Strawberry
Cheese	Milk (breast)	Sweet potato
Chestnut	Milk (cow)	Tea
Chicken	Milk (goat)	Tomato
Clam	Mustard	Turnip
Cocoa	Oat	Turkey
Codfish	Onion	Veal
Coffee	Orange	Walnut (English)
Corn	Oyster	Wheat (whole)
Crab	Parsnip	Wheat gliadin
Cucumber	Pea	Wheat globulin
Duck	Peach	Wheat glutenin
Egg-plant	Peanut	Wheat proteose
Egg-white	Pear	Wheat leucosin
	Pecan	
Beef serum	Chicken feathers	Mouse hair
Horse serum	Dog hair	Rabbit hair
Tobacco	Goose feathers	Sheep wool
Cat hair	Horse dander	

Staphylococcus pyogenes aureus	Streptococcus pyogenes 3-valent
Staphylococcus pyogenes albus	Streptococcus pyogenes viridans
Staphylococcus pyogenes citreus	Streptococcus pyogenes hemolyticus
Micrococcus tetragenus	Streptococcus alpha hemolyticus
Micrococcus catarrhalis	Pneumococcus 4-valent
	Diphtheroid

On carrying out the cutaneous tests it was found that the only proteins he was sensitive to were *rye* and *wheat* and *wheat globulin*. Wheat leukosin, wheat proteose, wheat glutenin and wheat gliadin were all negative. The interesting fact is shown that this person is sensitive only to proteins of the rye and to wheat globulin, the other proteins of wheat not causing any reaction. We therefore have a case of a baker sensitive to the proteins of rye and wheat, proteins with which one may say he spends a great deal of time.

Cases showing the relation between occupation and bronchial asthma are not common. The following quotation from Walker[3] is of interest in this connection:

"Occupation may have a direct bearing on the cause of bronchial asthma, and occupation frequently explains the development of sensitization after the age of forty. This occurrence, however, is not usual. Of 11 patients who became sensitive to proteins after the age of forty, 4 were bakers and sensitive to wheat protein, 1 was a hostler and sensitive to horse dandruff protein and 1 was a sifter of green coffee beans and was sensitive to green coffee protein, therefore in over half of these cases occupation was responsible for the cause of the asthma. Three unusual instances where occupation bore a direct relationship to the cause of the asthma are sufficiently interesting to mention. A man whose work consisted of sifting green coffee beans became sensitized to the proteins in the green husks and had asthma from the protein. Another man whose work was that of a jewel polisher became sensitive to the proteins in the dust from boxwood with which he polished the jewels, and a second man, working in the same room, became sensitive to the dust from the orangewood with which he polished jewels. The man sensitized to the boxwood was not sensitive to the orangewood, and *vice versa*."

As regards the treatment of these cases one can proceed in anyone of three ways: (1) The offending protein must be eliminated, that is, it must not be taken in the diet and the occupation must be changed so that the offending protein will not be inhaled. (2) If the protein is only offending on account of the ingestion of the same it can still be taken in the diet, but it must be only used after it has been subjected to a high heat. For example, it is known that patients who are sensitive to potato protein are usually able to eat baked potato, although boiled potato causes symptoms. Raw milk may cause symptoms in patients sensitive to milk protein, but boiled milk will not. Shredded-wheat biscuits and thin slices of bread well toasted on both sides may be eaten by patients sensitive to wheat protein, while the unheated wheat preparation would cause symptoms of ingestion. The explanation for these facts must be that the high temperature that the foods are subjected to destroys the anaphylactic properties of the protein contained in the same.

[3] Bronchial Asthma, The Oxford Medicine, 1919, ii, 128.

(3) Consists in treating or desensitizing the patient with those proteins that he has been found to be sensitive to by the skin or cutaneous test. One can give subcutaneous injections of the offending protein, but the procedure is difficult and not as satisfactory as the method of feeding the proteins. In this method gradually increasing doses of the offending proteins are fed until large amounts are taken without the production of symptoms. By this method of desensitization, Schofield,[4] Rich,[5] Schloss,[6] Talbot,[7] and Grover[8] have had successful results in children. Walker[9] states that he has tried this method of treatment with adults, but none have been conscientious enough to take the protein per schedule for any length of time.

EXPERIMENTAL CHRONIC SUPPURATIVE ARTHRITIS.

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Arthritis has been a subject for experimentation over a period of years, and during this time the effect on the joints by many organisms has been studied. The green streptococci have probably been most extensively used, and have produced the most interesting findings, with not only local joint changes, but, in addition, alterations in the heart, arteries and kidneys, constituting a combination of lesions which simulated not a little those observed in the complex known as acute rheumatic fever.

The character of the joint reaction caused by the Streptococcus viridans is of a comparatively mild type, subsiding usually in a relatively short space of time, with a variable grade of disability of the joint. Of the other organisms, the one that bears the most interest is the hemolytic streptococcus, and I wish here to describe some observations made on rabbits treated with a member of this group.

The single strain of streptococcus used in these experiments was isolated on January 8, 1919, from the pus of an abscess in the submaxillary gland in a psychopathic patient who died eight days later of pneumonia. Permission for an autopsy was not granted. It may be stated, however, that during life the patient presented no evidence of bone or joint involvement. The organism in question was

[4] Lancet, 1908, i, 716.
[5] Jour. Michigan State Med. Soc., 1914, xiii, 649.
[6] Am. Jour. Dis. Children, 1912, iii, 341.
[7] Boston Med. and Surg. Jour., 1916, clxxv, 191.
[8] Reported by Walker (loc. cit.).
[9] Loc. cit.

a Gram-positive coccus arranged mostly in chains of five or six, but at times with as many as ten cocci in a chain. There was no tendency to an arrangement of the cocci in pairs within the chains. On blood-agar it grew in a small, shiny, nipple-like colony, with a distinct, clear zone of hemolysis. Fermentation of lactose and salicin with negative results on mannite and inulin, placed the organism in the class of the common Streptococcus pyogenes (Holman). With a streptococcus at hand which had caused a local submaxillary abscess in a human, and showing relatively low virulence, it was deemed a favorable opportunity to study the effect of this organism on rabbits. With the aim in view of preserving a possible elective affinity for the submaxillary gland the organism was cultured in columns of dextrose infusion broth 11 cm. high, and after forty-eight hours the organisms were removed by centrifugation and diluted so that each cubic centimeter represented 15 c.c. of the original culture. Of the thirty-four animals injected with this organism the following doses were given: 1 c.c. to two animals, 1.5 c.c. to 11 animals, 2 c.c. to 19 animals, and 2.5 c.c. to two animals; 26 animals received one injection and 4 each were given two and three doses respectively; 14 of these animals were injected with the original strain, 6 shortly after the organism was isolated and 8 after the organism had been kept three months upon culture media; 20 rabbits were treated with the organism after one animal passage, 13 from one animal and 7 from another. The symptoms presented by the animals following these doses were comparatively mild. Marked disturbances in the general physical condition of the animals were not observed and it was only after a period of several days or at times of several weeks before they showed any discomfort, and this was due to difficulty in locomotion brought about by joint involvement. The length of time that the animals lived following the treatment varied widely, ranging from three to eighty-seven days. One rabbit died on the third day, two on the fourth, five on the sixth, one on the seventh, four on the eighth, one on the ninth, three on the tenth, two on the twelfth, one on the fourteenth, one on the seventeenth, one on the twentieth, one on the twenty-first, one on the twenty-third, two on the thirty-third, one on the thirty-eighth, one on the forty-sixth, one on the sixtieth, and one on the eighty-seventh day. Four animals were killed respectively on the eighth, twenty-ninth, forty-seventh, and sixty-second day. The animals killed on the eighth and twenty-ninth days had been injected with the original strain, while those killed on the forty-seventh and sixty-second had been treated with the organism after one animal passage. The average number of lesions in six animals treated with the original organism was four while that in eight animals treated with the original organism after three months' artificial cultivation was eight. Six animals not included in this list are still living, four apparently well and the remaining two have joint involvement.

Of the first four, two received doses of the organism after one animal passage, while the other two received doses of the organism after three months' artificial cultivation. The remaining two of the six animals have enlarged joints. One of these animals was first injected on January 13 with 1.5 c.c. of the original organism and subsequently was given three doses, the last on April 8, 1919. The only joint enlargement that this animal showed occurred in the left ankle which was three times the size of the right, forming a large spindle-shaped, yellowish red swelling over which the hair was lost. At the present time the ankle has become considerable reduced in size and presents a rather firm, nodular outline. On March 7, the other rabbit was given 1.5 c.c. of the organism after one animal passage. This animal became quite sick and on April 8, showed a left elbow about three times the size of the right elbow and a marble-sized, yellowish red swelling behind both ankles. The hair was absent over all of these joints. At the present time these joints are still enlarged but, somewhat smaller than on April 8. They are boggy and show a yellowish red discoloration through the skin which is now slightly wrinkled over the joints. These animals recovered spontaneously without permanent joint injury.

The lesions produced by the injection of this streptococcus were almost entirely limited to the joints which, in order of frequency, were ankles[1] (21–22), fore-paws (19–16), wrists (16–16), knees (17–15), hind feet (18–13), elbows (10–8), shoulders (6–4), hips (left–1). An exudative lesion was found in the muscles of the leg thirteen times, in the forelegs nine, in the thigh and hip five, and in the back nine. A purulent reaction involving the epiphyseal cartilage of the head of the humerus was noted in two rabbits and a similar change was found at the junction of the ribs and costal cartilage in three animals. The kindeys, peritoneum, pericardium, and pleura were involved once in each instance, while the heart showed myocardial reaction in each of three rabbits without, however, visible changes in the valves.

The joint reaction consisted of a suppurative process characterized by more or less distention of the capsule with a creamy sticky fluid. In many instances there was an extension of the pus into the peri-articular tissues and frequently pus could be traced from one joint to another along the tendons and fascial planes with at times a suppurative involvement of the adjacent muscles. This reaction was noted in the case of the ankles and knee-joints and the wrists and elbows with also the pus following the tendons from the wrists and ankles respectively into the forepaws and feet. Again hemorrhage occasionally occurred into the subcutaneous tissue and muscles of the involved legs and a diffuse, jelly-like, subcutaneous serous exudate was not infrequently observed.

[1] The numbers in brackets after ankles, forepaws, wrists, etc., refer to left and right members respectively.

Smears from the pus in these joints showed many Gram-positive cocci in pairs and short chains with disintegrating endothelial cells and polynuclear leukocytes. However, in many smears no intact cells were observed but rather fragments of nuclei and finely granular debris. The organism injected was recovered in all instances from the joint exudate.

On gross examination the heart and kidney were found to be affected in but three of the animals. However, microscopical study of these tissues showed seven additional animals to have metastatic foci in the heart and kidney. The lesions in all ten of these animals were similar, consisting of areas of necrotic debris surrounded by large and small mononuclear leukocytes. These lesions were of the nature of chronic lesions rather than rapidly advancing abscesses seen in streptococcus infections. In the heart, calcified muscle fibers were seen in several instances with but slight evidence of inflammation. The areas in the heart muscle were commonly found well within the structure and had no particular relation to the endocardium or pericardium. In the kidney the lesions occurred, for the most part, in the medulla and involved the vessels coursing up in the columns of Bertini. They were similar to those observed in the heart with the exception that endothelial cells were more abundant. Embolic glomerular nephritis was not observed, although in several kidneys emboli of cocci were noted in the glomeruli without evidence of inflammation or hemorrhage. The lesions observed in the skeletal muscle were similar to those observed in the heart and kidney.

The literature dealing with the production of arthritis is copious and it is so well known that it is deemed inadvisable to review it at length. However, there are certain facts concerning the localization of organisms in joints that bear especial interest. We are particularly concerned with the peculiar predilection which this streptococcus exhibited for joints. In another paper we called attention to the frequency with which hemolytic streptococci could be isolated from the joints of animals which had been treated with such organisms. Usually hemolytic streptococci are so virulent that they rapidly produce a fatal septicemia which is not characterized by the focal lesions observed in more chronic infections but also in spontaneous human infections with the same organisms. The condition found is one usually associated with extensive hemorrhages. In such states even where there is no gross enlargement of the joints it is found that streptococci can be isolated in a large percentage of cases. Following the experimental administration of streptococci, all grades of inflammation may be seen from the initial congestion of the synovial membrane to the accumulation of the purulent exudate within the sac. The development of the purulent arthritis depends, however, upon the factors which determine the course of infections in general. The physical condition of the animals is very important and it is well known that animals in

apparently similar physical condition frequently react differently to the same organism administered under identical experimental conditions. If the dosage of an active organism is too large the protective mechanism of the body may not accomplish the destruction of the organism and as Bull has pointed out a fatal septicemia may develop. However, if the protective mechanism is competent to efficiently combat the progressive invasion of the offending organism, focal lesions only may develop particularly in the muscle where they grow and may later again be washed into the circulation.

Such focal lesions may arise in many locations although they are found more frequently in the heart, kidneys, joints, and muscles. At times the lesions in one of the above are more important than the others although all are involved in an appreciable percentage of instances.

Thus it would be difficult to ascribe to an organism a particular affinity for a given tissue unless the reaction is read in terms of intensity over and above that noted in other tissues. However, we do find evidence that certain organisms attack tissues with an apparent predilection as has been well demonstrated by Dick in his work on B. mucosus arthritis. Characters of this type remain permanent features of an organism and must not be confused with a degree of intensity of reaction which may appear as an elective affinity according to Rosenow.

It has been found possible to produce arthritis in sensitive joints. Within recent years, Herry and later Faber used the toxins of the streptococcus to sensitize the joint. Upon the injection of the streptococcus intravenously at a subsequent period, a definite arthritis was produced. In several animals that had recovered spontaneously from arthritis, Cole was able to provoke a relapse by another intravenous injection of the same streptococcus.

The streptococcus which we have isolated from an abscess of the submaxillary gland presented the unique feature of mainly attacking the joints of rabbits. It was found unnecessary to sensitize the joints and in most instances but a single dose was given to an animal. Further the animals remained in good physical condition and only experienced discomfort from the joint lesions. There was none of the emaciation which commonly occurs early in streptococcus treated animals and most of the animals survived the treatment for a variable number of days. It was only after the development of a well defined arthritis that the organisms again reappeared in the blood in sufficient numbers to cause death. The results obtained in the animals treated with this streptococcus are somewhat different from the picture usually seen in experimental streptococcus infections. In a previous article we recorded the results obtained from injecting rabbits with hemolytic streptococci. Twenty-five of fifty-eight animals gave positive postmortem cultures from the knee-joints but in no case was there a true suppurative arthritis. This

no doubt, was due to the virulence of the streptococci used, as most of the animals died within a period of a few days following the treatment. It may also be indicated that the striking feature in these animals was not the joint involvement but rather a picture of severe infection characterized by extensive hemorrhages.

At the time when the experiments were being conducted with the streptococcus from the submaxillary gland, twenty-five rabbits were used for controls. Fifteen rabbits were treated with hemolytic streptococci from pleural fluid. Five rabbits each were treated respectively with two strains of S. pyogenes and five rabbits received injections of a S. subacidus. Ten other rabbits were inoculated in series of five with two strains of S. pyogenes that were isolated respectively from a herniotomy wound and peritoneal exudate. The results obtained in these animals were in marked contrast to those animals inoculated with the streptococcus from the submaxillary gland in that they presented a hemorrhagic type of reaction similar to that which we had previously reported. These animals were from our own stock and apparently in identical physical condition. The doses administered to these animals were not excessive in that 1.5 c.c. were given to twenty rabbits and 2 c.c. to five rabbits. From these results it would appear that the qualities of this particular streptococcus are somewhat different from others which we have studied. It is difficult to understand why a streptococcus isolated from a human submaxillary gland should have a predilection for the joints of rabbits. It would seem that although this streptococcus showed a remarkable constancy in location and type of lesion produced, the location of the lesions in the animal had no relation to the origin of the organism or to the lesion produced by it in the patient from which the strain was obtained. Results of this kind limit the usefulness of experimental bacteriology for determining a possible tissue predilection for organisms of human origin.

Conclusions. From our study of this organism it would appear that we have a streptococcus of fairly low pathogenicity but of rather high invasive quality, which possesses the ability to attack the joints of rabbits and produce in them a chronic suppurative arthritis. This quality of attacking the joints was not lost after a period of three months' artificial cultivation. Although joints were mainly attacked, certain other tissues were involved an appreciable number of times. The organism was of human source, isolated from the submaxillary gland.

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BLOOD CHOLESTEROL IN GASTRO-ENTEROLOGIC CASES.[1]

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Cholesterol or cholesterin, a monatomic alcohol, is found as such in the human blood stream. In combination with fatty acids it forms, among other esters, cholesterol palmitate and cholesterol oleate. A fairly definite relation or balance is maintained between the free and combined cholesterol of the blood. Cholesterin is also found in the nervous system, bile, milk and other body tissues and fluids. There is some uncertainty as to the exact chemical structure of cholesterol.[2] It is soluble in ether, chloroform, benzene, fats and hot alcohol.

The origin of cholesterol is, for the most part, exogenous, although there is some evidence that it may have an endogenous source.[3] It is readily absorbed from the intestinal tract contents through the chyle and may be recognized free or esterized in the contents of the thoracic duct.[4] The blood cholesterol content can be readily increased by feeding foods rich in this substance. That the biliary cholesterol can be increased in like manner remains uncertain. Feeding experiments leave this point in doubt. The origin of biliary cholesterol is perhaps to be found in the disintegrating blood cells of the body. Bile is the only suitable solvent in the body for cholesterol, but whether the bile is a normal mode of excretion for this substance is just as uncertain as other facts pertaining to this alcohol. Fistula bile is poorer in cholesterol than gall-bladder bile, and some, therefore, believe that this substance somehow or other has its origin in the lining membrane of this organ. Some contend that this difference in the bile from these two sources soon ends after the unusual conditions imposed by the operation cease;[5] recently, Rous and McMaster[6] seem to have demonstrated an ability on the part

[1] Read before the American Gastro-enterological Association, May 3, 1920.
[2] Hawk: Practical Physiological Chemistry, 5th edition, p. 355.
[3] Klein: Biochem. Zeit., 1910, xxx, 465.
[4] Mueller: Jour. Biol. Chem., 1910, xxii, 1.
[5] Rothschild and Wilensky: Am. Jour. Med. Sc., vol. clvi, p. 2.
[6] Proc. Assn. Am. Phys., 1920.

of the gall-bladder to withdraw normal salt solution from the hepatic bile and thereby concentrate the latter fluid. There is no reason to believe that cholesterol is changed to cholic acid, a substance participating in the formation of bile salts. The liver probably is the regulator of cholesterol metabolism and maintains the level by excretion through the bile.[7]

Both lecithin and cholesterol assume some role in the transportation and metabolism of fats. The esters of cholesterol are found in the red cells and are practically absent during fasting. The presence of this substance in the red cells probably accounts for the role the latter play in fat metabolism.

The amount of cholesterol normally found in the blood has been variously stated. Bacmeister and Havers[8] give 110 to 180 mg. per 100 c.c. and Widal, Weill and Laudat[9] 174 to 195 mg. per 100 c.c. Bloor[10] found the average value for men to be 210 mg. and 230 mg. for women. A wide variety of normals are given by other workers. It is probably fair to say, however, that an upper normal is about 200 mg. per 100 c.c. of blood while the lower level is about 150 mg.

The literature is in accord on the findings of a low blood cholesterol in pernicious anemia which probably has its basis in the diminution of the corpuscular elements to be found in this disease. To beriberi, syphilis, prostration, cachexia and fever are accredited low cholesterol findings, and recently a low blood cholesterol[11] has been found to be of bad prognostic import in nephritis. In non-grave nephritis, arteriosclerosis, obstructive jaundice, diabetes and pregnancy high figures are said to prevail. The literature is by no means in accord as to the constancy of blood cholesterol content in these conditions, and of no disease is this truer than of cholelithiasis. There are those who publish almost constant hypercholesterinemic figures[12] for this disease, while others have had very irregular results.[13] [14]

In the winter of 1916–1917, hoping that a determination of the cholesterol content in the blood of gastro-enterological patients would help in diagnosis, especially when the biliary system seemed to be in question, it was planned to examine a series of cases in this way. The Bloor[15] method was employed. Whole blood was used and it was obtained during the morning hours. After a prolonged interruption in the work the number of patients so investigated reached sixty and the number of blood cholesterol readings seventy-five in these cases.

In this group two cases of diabetes showed 160 and 151 mg. from

[7] Rothschild: Proc. New York Path. Soc., December, 1914, N. S., xiv, 229.
[8] Deutsch. med. Wchnschr., 1914, p. 8.
[9] Soc. Biol., 1911, lxiv, 883.
[10] Jour. Biol. Chem., 1916, xxv, 577.
[11] Henes: Arch. Int. Med., April, 1920, xxv, 4.
[12] Henes: Jour. Am. Med. Assn., 1914, lxiii, 146.
[13] Gorham and Meyers: Arch. Int. Med., October, 1917, xx, 4.
[14] Denis: Jour. Biol. Chem., 1917, xxix, 93.
[15] Jour. Biol. Chem., 1916, xxiv, 229.

100 c.c. of blood, while a third case yielded values of 241 and 304 mg. The latter case has a gall-stone history and corresponds in type, but the presence of calculi has never been established. These cases exhibited no acidosis.

Two cases of pernicious anemia showed 139 and 105 mg. Both of these cases presented an achylia gastrica, and it must be assumed that the upper abdominal symptoms here in all probability were gastric in origin. The well-known antihemolytic powers of cholesterol are to be considered in connection with the anemias, and these low figures are interesting in this light. Surroeo[16] contends that cholesterol findings in the blood are a measure of the state of the organic defences, and he is not alone in this opinion. Findings below 129 mg. show a weakness in this respect according to this Frenchman and findings above 200 mg. indicate a slow infection of some type. Findings below 100 mg. are of bad prognostic character.

Assuming that the leukocyte count is a measure of organic defence or an index to the presence or absence of infection we found that the low leukocyte count cases in our series averaged 202 mg. of cholesterol while the increased leukocyte cases yielded an average of 220 mg. A case with only a transient gastro-intestinal upset gave findings of 363 mg. and 336 mg. of cholesterol and had but 5000 leukocytes. Our lowest cholesterol finding was in a case with 100 mg., and white cell counts of 9100 and 10,000. None of our low cholesterol cases appeared to be in grave danger nor to be lacking in defence reactions.

Carcinoma and cholesterol, according to some, present an interesting relationship. Luden[17] reports a high cholesterol content in carcinoma and that cholesterol promotes cell multiplication, especially cells of the malignant variety. Our two cases of carcinoma showed readings of 120 and 180 mg.

Four jaundice cases were of the catarrhal variety and yielded 144, 143, 214 and 171 mg., while a single obstruction case showed 330 mg. This accords with the findings of Rothschild and Felsen,[18] who report high findings in the obstructive jaundices.

In gastroduodenal ulcer our findings were 166, 169, 176, 115 and 250 mg. per 100 c.c. of blood. In three of these cases the diagnosis was made clinically while in one the lesion was found at operation and the other showed a filling defect on roentgen-ray examination.

Intestinal stasis cases apparently uncomplicated yielded the following findings: 279, 172, 136, 125, 108, 180, 480 and 125 mg. per 125 mg. per 100 c.c. of blood. In one case three observations were made of 185, 196 and 240 mg.

In this group of 60 cases, 36 were constipated and addicted to the cathartic habit. Their average cholesterol reading was 226 mg. The highest figure was 440 mg. and the lowest one 100 mg. Those

[16] Ann. de la Fac. de Méd., Montevideo, December, 1917.
[17] Jour. Lab. and Clin. Med., December, 1917, p. 3.
[18] Arch. Int. Med., November, 1919, xxiv, 5.

with regular daily movements of the bowels were 16 in number and averaged 183 mg. Three cases with loose, somewhat frequent movements averaged 295 mg.

In cases diagnosed as gastric neuroses of the hypersecretory variety, findings of 160, 185, 200 and 154 mg. were found. One of these cases with 440 mg. was negative in a gastro-intestinal calculus roentgen-ray examination.

A study of the gastric contents of these 60 cases showed that 28 had a high acid curve. Their average cholesterol reading was 218 mg. The normal acid cases numbered 12, with an average reading of 220 mg. Achylia gastrica cases averaged 178 mg. while those with low acid curves showed 184 mg. per 100 c.c. of blood.

In 5 chronic appendicitis cases we found 180, 190, 223, 285 and 318 mg. of cholesterol in 100 c.c. of blood. The last two were operative patients in whom the biliary apparatus was declared negative, but with the appendicular condition there existed widespread adhesions throughout the right abdomen.

The following isolated diagnoses were made in cases with their respective cholesterol readings:

Gall-bladder disease, sine calculus (operative)	149, 195
Rheumatoid arthritis	187
Chronic pancreatitis	248
No abdominal lesion (operative)	286, 147
Visceroptoses (2)	235, 216
Migraine and hypertension	210
Abdominal adhesions (operative)	100

The relationship of cholesterinemia and gall-stones in our cases is shown in this table:

Gall-stones (clinical).	Gall-stones (operative).
206	250
151, 333	190
250, 280	200
316	

Gall-stones (roentgen ray).	Passed stones per bowel.
136	210
200, 220	122
260	After passage of stones, calculus roentgen-ray negative.
222	
284, 160	
177, 260	
310, 232, 250	
260	
270, 182	

Bracketed figures represent findings in the same case.

The question of the relationship of cholesterol and gall-stone formation has been much discussed in the literature. For the most part the evidence points to an inconstant and uncertain status. Reiman and Magoun[19] in a study of 60 operative cases found that other upper right abdominal lesions yielded cholesterol figures almost as high as those obtained in stone cases, both averages being above normal. Gorham and Meyers[20] and Denis[21] are in accord that a cholesterol estimation has little clinical and prognostic value in calculus cases.

Obviously there is no reason to assume a hypercholesterinemia in stones of other than cholesterol composition. It must also be true that the precipitation of cholesterol cannot be a uniformly progressive procedure if it depends largely upon an exogenous origin in the blood or bile; that even though a stone were one of hypercholesterinemic origin, findings in the blood would not always show high readings for this lipoid. When one subtracts the instances when stone formation has an infection or stasis origin we add still further to the instances when biliary calculi might be present without a hypercholesterinemia. If we consider the weight of gall-stones and add the amount of cholesterol in the bile, together with the length of time required for their formation, it seems only reasonable to assume abnormal conditions of crystallization and precipitation as etiologic factors. The causes of crystallization seem to be found in nuclei of bacteria or epithelial cells.

Whether a hypercholesterinemia can be caused by a lesion of the biliary system in turn due to the presence of stones is uncertain. That lesion could scarcely be anything else than an inflammatory one, and it is well known that stones may exist without inflammation, and inflammation along the biliary tree can be very extensive and severe without calculus formation. The relationship of gall-stones and cholesterol in the blood seems to be a complicated one—one which is intimately related to a complex of food, bile, blood and body tissues—their amount, chemistry, bacteriology and physical properties.

Summary. 1. Sixty cases presenting gastro-enterologic aspects were studied for their blood-cholesterol content.

2. Insofar as possible the clinical, roentgen ray and postoperative findings are correlated.

3. The relationship of constipation, hyperacidity and leukocytosis to cholesterol findings are considered.

4. The highest finding was 480 mg., the lowest was 100 mg.

5. Inconstant results were obtained in most of the conditions when more than one case was studied.

6. The figures for cholelithiasis averaged high (228 mg.). Other cases averaged 207 mg., both averages being above the high normal

[19] Surg., Gynec. and Obst., March, 1918, p. 282.

[20] Loc. cit.

[21] Loc. cit.

limit of 200 mg. The highest finding was 316 mg. and the lowest 136 mg. The highest reading in non-calculus cases was 480 mg. and the lowest 100 mg.

7. Inconstant findings were sometimes found when more than one estimation was made in the same case on different days.

Conclusions. From our limited studies and an estimate of the literature, blood-cholesterol seems to offer little practical diagnostic help in gastro-enterological cases.

Appreciation is expressed to Dr. Joseph Sailer for the use of clinical material and to Miss Sarah C. Hetherington for her valuable assistance.

A STUDY OF HYPERACIDITY.

By Martin E. Rehfuss, M.D.,

and

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Philadelphia, Pa.

Hyperacidity is a subject which has received an endless amount of discussion. In fact the main portion of this subject has been thoroughly incorporated into the body of clinical medicine without the thorough investigation which the subject deserves. In other words the subjective symptom hyperacidity is a definite clinical entity. Less definite, but none the less fixed in the minds of the medical profession, is the belief that there exists an actual demonstrable titratable acidity. In fact the tremendous amount of clinical work which has been performed on pathologic cases has firmly fixed in the eye of the clinician the fact that high acid figures demonstrate gastric pathology. There was absolutely no evidence at hand to counteract this tendency until a more thorough research into normal gastric activity was carried out. The whole subject, therefore, reverts to the question of a comparison of normal and pathologic findings, and it requires, as a *sine qua non*, an absolute determination of gastric activity and the factors controlling it in health. We must start in with a normal conception before we attempt the interpretation of pathologic data.

We deny that most of the known information on gastric function was obtained on normal individuals, otherwise it is not possible to understand the marked discrepancies which have occurred in this line and which have occasioned so much discussion among gastro-enterologists. An individual with a gastric fistula is not a normal individual; an animal with a Pavlov pouch is not a normal animal; single studies on isolated individuals do not reveal the variations

and normal tendencies which attend gastric digestion. In fact, we know of no series of investigations previous to our own in which a large number of normal individuals were submitted to examinations destined to reveal the whole range and variations of the gastric response to every form of foodstuff.

The results of these investigations, some of which have been published, establishes clearly the following facts, which are of extreme importance in establishing a normal conception of gastric digestion:

Every individual has a characteristic form of gastric digestion.

We would divide this statement into two parts: First, there are apparently three forms of secretory response, all of them found in normal individuals. Secondly, there are three forms of motor response also found in the same individuals. We have already described the three varieties of secretory function as hyper, iso and hyposecretory function. In other words, all individuals belong in one of these three groups, and, as a rule, an individual who shows a hyposecretory response with one type of gastric stimulus (food) will show it with another type of stimulus. About 40 per cent. of normal individuals reveal a response in the hypersecretory group and about 30 per cent. in the iso and hypersecretory groups respectively. An individual in health with conditions equal almost always runs true to type; in disease there may be marked variations, as we shall discuss in later communications. In other words a hypersecretory individual will react in hypersecretory fashion to water, bread, meats and, in fact, the whole line of foodstuffs, while the hyposecretory individual will react in hyposecretory fashion to the same stimuli.

Not only is there a definite form of reaction to a response, but there is also a more or less typical form of motor response, so that we have been able to group our cases into those who from the motor standpoint reacted: (1) rapid evacuation or rapid or quickly emptying stomachs; (2) slowly evacuating stomachs or the hypomotile types; (3) those which empty neither fast nor slow, but, are according to our conceptions, of normal function. We might divide these types into hypermotile, hypomotile and isomotile types, inasmuch as they represent ranges of normal gastric action. In other words, there is unquestionably a large secretory and a large motor range in health which must be thoroughly understood before we draw pathologic interpretations from data which may yield similar figures.

There is no question that exaggerations of almost all of these types may indicate pathology, and the line of demarcation between the end of normal findings and the beginning of pathologic manifestations is exceedingly difficult to define. Furthermore, we know that gastric pathology may exist in the presence of normal secretory and motor function or may convert one type into the other type and

still be within the range of normal function. But another interesting point is evident from these studies, namely, the fact that it is only a step from these normal findings to obviously pathologic ones. For instance the findings of the hypersecretory type may be exaggerated into pronounced hypersecretion. In discussing hypersecretion elsewhere one of us pointed out that hypersecretion, or rather a continued secretion after all digestion had ceased in the stomach, was a frequent finding in the hypersecretory normal type and that it was difficult to establish the point at which normal continued secretion ceased and pathologic hypersecretion commenced. The fasting hypersecretion, Reichmann's disease and digestive hypersecretion, are but exaggerations of the hypersecretory type, while hypersecretory findings in the other two types are at once abnormal. Likewise it is but a step from the hyposecretory normal types to the phenomena subacidity, anacidity, achylia and delayed digestion. Disease in its effects on gastric function apparently follows these steps.

The subject which we wish to discuss, however, is the question of hyperacidity, and here we are immediately met with the fact that in discussing this subject correctly we must immediately separate the symptom hyperacidity from the true hyperacidity as revealed by chemical titration. In no way does the symptom of hyperacidity as described by the patient come into this discussion. We are all of us clearly established as to the fact that the subjective symptom hyperacidity in many instances has nothing to do with titratable acidity. This symptom has repeatedly been noted in the presence of gastric achylia, and one of us has encountered many cases of demonstrable subacidity in which the patient complained of hyperacidity and was relieved by the administration of alkalies. Here we meet with a condition which is clearly a lessening of acid tolerance. One thing is clear clinically, that many subacid cases reveal this symptom, and not a few cases in which high acid figures are found are absolutely without any evidence of this finding (subjective); on the other hand a different mechanism, a marked increase in secretory velocity, with an excessive amount of unsaturated secretion (hypersecretion), may and frequently does induce this symptom. But none of these conditions are to be called true hyperacidity.

Pinning ourselves down to exact facts as revealed by the titration of the gastric contents at intervals, what then are the findings? In the first place hyperacidity clinically is taken as being present when the titratable acidity exceeds 70 to 80 (0.25 to 0.28 per cent. HCl) and yet in over 40 per cent. of our normal cases the total acidity exceeds this figure. In our series of cases the average total acidity encountered in a series of studies on foods in the normal individual was as follows:

RESULTS OF EXAMINATION OF 924 COMPLETE CURVES OF VARIOUS FOODS IN THE NORMAL HUMAN STOMACH.

Food.	Total number of cases.	Cases with acidity of 100 or over. Number of cases.	Percentage.
Bread and cereals	82	6	7.3
Pies, cakes and pastry	89	35	39.3
Fish	82	75	91.5
Meats	203	156	76.8
Ice-cream and drink	48	10	20.8
Eggs	104	23	22.1
Nuts and fruits	94	34	36.1
Tea	139	27	19.3
Milk and cream	47	21	44.6
Candy	39	3	8.0

NORMAL ACID FINDINGS (842 CURVES).

384 cases out of 842 had an acidity of 100 or over.

Acidity of 200 or over	1 case
Acidity of 180 or over	2 cases
Acidity of 170 or over	4 cases
Acidity of 160 or over	11 cases
Acidity of 150 or over	35 cases

35 cases in 842 had an acidity of 150 or over; all of these belonged to the meat, milk and fish group.

A study of these facts enables us to make the statement that to our knowledge and in our experience there is no range of titratable acidity pathologically which cannot be found normally under certain circumstances. An acidity of 100 or over (0.36 per cent. HCl) is frequently encountered normally and is not to be construed as hyperacidity. In fact, with certain foods (notably meats and fish) the average was considerably over 100, while with other foods the secretory output was below this point. Immediately the clinical objection is interposed that inasmuch as we use one form of meal as a standard, what are the normal variations of such a meal? The normal variations with tea and toast, for example, are such as to preclude the possibility of accepting our present conception of hyperacidity as the correct one. Furthermore, while the higher acidities occur with protein foods, for example, and there is an unquestioned range of secretion and secretory output varying with different foods, the individual who may register normal acidities with carbohydrates may show hyperacid figures, with protein foods in both instances and with no evidence of gastric pathology.

These findings are so important, and have been so thoroughly impressed upon us by our work, that we do not hesitate to say that hyperacidity as expressed by an actual increase in titratable acidity over the normal range scarcely exists, inasmuch as we have obtained in our normal studies on normal men figures which overlap any obtained under pathological conditions.

This does not mean, however, the volume of the secretion, inas-

much as the total amount of acidity and not the degree of titratable acidity may vary markedly from normal findings.

Pathologically, therefore, it is evident that if the normal range of titratable acidity for a certain foodstuff is to be found within certain limits these limits may be exceeded in diseased conditions. Furthermore, it is evident that if an individual who is normally hypersecretory in type begins to show hyposecretory responses, this may be construed as evidence of the onset or presence of gastric pathology.

On the other hand very high acidities, such as 0.5 per cent. HCl, when introduced into the stomach are reduced to the gastric optimum by means of the autoregulatory mechanism, namely, the regurgitation of the alkaline intestinal secretion.

In other words, in health, while the variations in titratable acidity are very much higher than has hitherto been assumed, nevertheless, there is unquestionably this mechanism, which not only protects the organ but which ensures the presence of a gastric optimum at all times. A disturbance of this mechanism will naturally result in high acid figures, and in most cases subjective symptoms. It was the evidence which we have enumerated above which led us to publish some time ago the paper on the presence of the secretion of juice of constant acidity in man similar to that described by Pavlov in laboratory animals, and there is much to make us believe that the slow rise and fall of the curve are explained by many physical and chemical factors which alter this curve.

In the analysis of the components making up the gastric secretion we must clearly distinguish between the active digestive phase in response to food and the phase of the fasting stomach in which a very different mechanism is at work. Our work clearly establishes the fact that the digestive phase is made up of the psychic and chemical secretions. The psychic secretion begins immediately in response to the sight, taste and odor of food and continues for sixty to eighty minutes, possibly throughout the entire digestive period. In health with a mixed meal the quantity of secretion is over 200 c.c. and the average acidity in our first series of experiments with the psychic secretion was an average total acidity of 97.6 (0.35 per cent. HCl). The chemical secretion begins very early in digestion, probably in response to the absorption of secretagogues or soluble digestive products formed by the action of the existing secretion or psychic secretion on the food in the stomach; it is more persistent and continued and lasts throughout digestion, frequently persisting after food has left the stomach (postdigestive hypersecretion or continued secretion). There is clearly in response to food a marked increase in secretory velocity which only slowly reaches its height, owing to the fact that secretory velocity gradually increases and because the initial acid output is probably partially neutralized by the food. How great this is can be realized by the fact that small therapeutic doses of hydrochloric acid have no

appreciable influence on the gastric curve, and in the study of one case of anacidity more than 250 c.c. of 0.25 per cent. HCl had to be introduced into the stomach to induce a curve which at all resembled the normal one. It is therefore evident that the introduction of food is followed by the presence of marked secretory activity, a factor which is disturbed or perverted in disease. On the other hand the fasting stomach presents other phenomena. There is clearly a marked lessening in the velocity of the secretory output. Active peristole function succeeds peristalsis. The total and free acidity fall and through the patulous pylorus ready regurgitation occurs, with the increase of alkaline duodenal secretion, while in 55 per cent. of normal cases the fasting stomach shows the presence of bile. These succeeding cycles, the digestive and interdigestive cycles, follow one another in regular fashion and the factors controlling them are those enumerated above.

In conclusion we may state:

1. Hyperacidity as discussed in this article does not refer to the subjective symptoms, but the objective finding of an actual increase of titratable acidity over normal.

2. Evidence is deduced to prove that the normal individual elaborates acid figures as high as those commonly associated with pathologic syndromes, and in our experience no acid figures found in disease have exceeded the figures which we have obtained under certain circumstances in health.

3. The average acid finding during the digestion of certain foods in the normal stomach was found to be within the range which is accepted by all clinicians as abnormal.

4. There is a group of normal individuals, approximately 40 per cent., who constantly show the acid titration findings of so-called hyperacidity.

5. It is essential that our views on this subject be altered and that we accept first these normal findings as a basis for the interpretation of pathological cases.

6. The introduction of very high acidities (0.5 per cent. HCl) is followed by the activity of the autoregulatory mechanism which brings about a gastric optimum.

REVIEWS

A Laboratory Syllabus of Clinical Pathology. By Charles E. Simon, M.D., Professor of Clinical Pathology in the School of Medicine and the College of Physicians and Surgeons of the University of Maryland. Pp. 86. Philadelphia and New York: Lea & Febiger.

Teachers of clinical pathology will find this syllabus of great value; the student will likewise appreciate the clear and explicit directions. It is not a text-book but strictly a laboratory manual, prepared by the author for the express purpose of aiding the teaching of an important practical subject and serving as a time-saver in view of an overburdened curriculum. The subject of examination of the blood, urine, sputum, stomach contents, spinal fluid, Wassermann test, blood sugar, blood urea, etc., are covered in thirty-nine lessons of about two hours each; doubtless most teachers will find it necessary to repeat portions of several lessons. The book could be improved upon by giving the subjects of the lessons in bold type in the text, in addition to the table of contents.

J. A. K.

Pathogenic Microörganisms. By William Hallock Park, M.D., Professor of Bacteriology and Hygiene, University and Bellevue Hospital Medical College, and Anna Wessels Williams, M.D., Assistant Director of the Bureau of Laboratories of the New York Department of Health; assisted by Charles Krumwiede, M.D., Assistant Director of the Bureau of Laboratories of New York. Seventh edition. Pp. 786; 214 engravings; 9 full-page plates. Philadelphia and New York: Lea & Febiger, 1920.

This book scarcely requires any further comment than the statement that it is a worthy successor of the preceding six editions; it is so well and favorably known and so widely used that nothing remains to be written about it except to commend the authors for drawing upon the valuable experience and work of Dr. Krumwiede and other laboratory associates.

Considerable new material has been added and portions entirely rewritten. The information gained during the influenza epidemic

and during the last part of the war with preventive measures against typhoid fever, paratyphoid fevers and wound infections due to anaërobes has been added. The chapters on media, immunity, streptococci, yeasts and influenza bacilli have been extensively revised, bringing the book quite well up to date and presenting the subject-matter in the clear, concise and systematized manner characteristic of all editions of this valuable book. J. A. K.

SURGICAL CLINICS OF CHICAGO. Volume IV, No. III, June, 1920. Pp. 204; 79 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS number is somewhat smaller than the previous ones, having fewer articles, but with the one criticism of a mistake in assembling of the book, it reaches the high standard set in the past. The error in binding spoils to a great extent two of the contributions.

The first article on empyema brings out some valuable points even on this much discussed subject. The illustrations here are also very good.

Another writer gives a very instructive contribution on the common bile duct and the means of surmounting many of its operative difficulties.

Other articles, though shorter and on less spectacular subjects, give the reader valuable points. E. L. E.

MENDERS OF THE MAIMED. By ARTHUR KEITH, M.D., F.R.S., Conservator of the Museum and Hunterian Professor, Royal College of Surgeons, London. Pp. 335; 23 illustrations. New York and London: Oxford University Press.

BY weaving together accounts of the lives and of the works of eminent men of science who have advanced the knowledge of surgery during the last century and a half, Professor Keith has produced a highly interesting volume. Entertaining when viewed as a series of surgical biographies, including John Hunter, Hilton and H. O. Thomas, it is also valuable from the scientific side, for by making use of these personalities and their endeavors the author has traced the growth of our knowledge on such important subjects as degeneration and regeneration of nerves, bone-growth and bone-reproduction and tendon-transplantation. There is a freshness and vigor in the style, and the author succeeds in illumining for us many of the critical situations in surgical history from which advances

were made. To achieve this he introduces us to various workers in their hospital wards, physiological laboratories, dissecting rooms or private workrooms, and graphically delineates the environment in which they worked and the problems which confronted them. Thus we have Duchenne and his battery in the Paris hospitals, testing the action of muscles; we have Waller studying the nerve of the transparent tongue of the frog, which resulted in establishing the law of Wallerian degeneration; we have Arbuthnot Lane, at Guy's Hospital, performing his first osteosynthesis; we have Henry Head submitting to have certain nerves cut in order to follow out more closely the loss and reacquirement of sensibility. Not only, however, are we shown the bright side of the picture, for in such a retrospect it is not uncommon to find at times the ruling point of view was erroneous, and we are made to realize by what uncertain steps knowledge progresses.

There is an interesting chapter on orthopedic work in the United States. This begins with an account of John Rhea Barton, professor of surgery in the University of Pennsylvania who in 1826 introduced a new operation on a case of ankylosis of the hip-joint. This and other novel operations indicate that already in the early years of the nineteenth century there was a native school of American surgery. In passing, one notes what long periods of time some of the older men spent in the dissecting room before entering on their surgical careers, *e. g.*, John Hunter, twelve years, and Hilton, twenty years.

This, then, is a history both of men and of ideas, and this fact, coupled with the author's realistic style, will ensure a wide circle of interested readers. W. H. F. A.

THE MORPHOLOGY AND EVOLUTIONAL SIGNIFICANCE OF THE PINEAL BODY. By FREDERICK TILNEY, M.D., Professor of Neurology, Columbia University, and LUTHER F. WARREN, M.D., Professor of Medicine, Long Island College Hospital. Pp. 257; 97 illustrations. Philadelphia: Published by the Wistar Institute of Anatomy and Biology.

THIS memoir is the first part of a review of the recorded facts about the pineal body. Part II deals with the physiology and pathology of the organ and Part III with the clinical aspects. The chief question of interest which is discussed is whether the Mammalian pineal body is to be regarded as a vestige or whether it is an organ in some way related to metabolism. Before discussing this and other related questions the comparative morphology, embryology and histology of the epiphyseal complex are detailed. In this descriptive part, which occupies nearly 200 pages, and in which 432 titles are quoted, a very thorough abstract of the literature is

given. In the last fifty pages of the volume the significance of the various facts is closely analyzed, with the conclusion that the pineal body cannot be a vestige but is a glandular structure necessary, in some way yet unknown, to metabolism. They conclude also that there is no direct relation between the median eye of reptiles and the pineal body of mammals, and that the latter cannot be regarded as the vestigial, metamorphosed or atrophic residuum of the former.

W. H. F. A.

PRINCIPLES AND PRACTICE OF INFANT-FEEDING. By JULIUS H. HESS, M.D., Professor and Head of the Department of Pediatrics, University of Illinois College of Medicine, etc. Second revised edition. Pp. 343; 18 illustrations. Philadelphia: F. A. Davis Company.

THERE is always need for a good book on infant-feeding. Dr. Hess's book is certainly in that class. It is not only good but it is a safe book to recommend to students and general practitioners who are not essentially pediatrists.

As usual one finds in the beginning of the volume general considerations including a discussion of the anatomy, physiology and bacteriology of the digestive tract and the metabolism of infants. In Part II the nursing and the management of the breast-fed infant are considered, and there is also a valuable chapter on premature infants. Part III deals with artificial feeding. All so-called methods of feeding are spoken of and impartially noted. Wisely, then, the author shows how they may all be used to advantage and combined in a complete study of an individual case. That is, one should know not only the calories and percentages in a mixture, but should also be aware of the number of grams of protein, fat and carbohydrate. In the last part of the book the various nutritional disturbances in artificially-fed infants are taken up in detail.

A. G. M.

OTO-RHINO-LARYNGOLOGY FOR THE STUDENT AND PRACTITIONER. By W. GEORGES LAURENS, authorized English translation of the second revised French edition, by H. CLAYTON FOX, F.R.C.S., with a foreword contributed by J. DUNDAS GRANT, M.A., M.D., F.R.C.S. Pp. 592; 324 illustrations. New York: William Wood & Co.

IT is always interesting to see the appearance of a book that endeavors to fill a new field, and the present treatise is, as far as we know, the only work devised solely for the instruction of the general practitioner who has not made oto-laryngology a special study. The

author, while instructing the general practitioner in "what not to do" and "what to do" in treatment of diseases of the ear, nose and throat, draws the line at that point where he believes a special training necessary to successfully handle this class of cases. The methods of examination are simplified and the more complicated ones only mentioned in order to show what can be done in such cases by a trained specialist. This is also true of the operative work, the minor operations being described in sufficient detail to enable their successful carrying out by the general practitioner, and the more complicated procedures simply mentioned. Yet we must admit that in trying to simplify the technic and methods used in the examination and treatment of diseases of the nose, throat and ear the author has perhaps in some instances overstepped the boundary and in others given what seems to us unwise advice. For instance the suggestion that deafness may be properly treated by the general practitioner, when it is admitted that a proper diagnosis of the condition requires special training, would seem to us pregnant of distinct harm. Also some of the operations which he describes such as the blocking of the superior laryngeal nerve for the pain of laryngeal tuberculosis, had much better be left to the specialist. Again, the advice that the removal of tonsils with punch forceps "is a method so simple as to be within the power of every doctor to practice" is very bad advice.

The ground covered is very extensive, and there is little doubt but that the usefulness of the average practitioner will be greatly enhanced by the reading of this work, and we believe that H. Clayton Fox, in translating it into English, has brought an important contribution to the medical literature of this country. The illustrations are largely diagrammatic, but numerous and exceptionally illustrative. G. B. W.

DISEASES OF THE THROAT, NOSE AND EAR. FOR PRACTITIONERS AND STUDENTS. By W. G. PORTER, M.B., B.Sc., F.R.C.S. (Edin.). Third edition, fully revised under the Editorship of A. LOGAN TURNER, M.D. (Edin.), F.R.C.S. (Edin.); Consulting Surgeon, Edinburgh Eye, Ear and Throat Infirmary, etc. Pp. 300; 79 illustrations, 44 of which are in colors. New York: William Wood & Co.

THE second edition of this little manual was published while the author was in active service with the British Army in 1916, the revision being undertaken by Dr. P. McBride. Major Porter, D.S.O., was killed in action in 1917 and the present edition has been carefully rewritten by Drs. J. Milne Dickie, J. S. Fraser, Douglas Guthrie, W. T. Gardiner and A. Logan Turner, which fact should speak for itself as to the value of the work.

It is essentially a book for the general practitioner, the senior student and the non-specialist, the major operations not being described in detail, the indications for their performance and their general features alone being given. Anatomical descriptions and illustrations of instruments have been omitted, which is a commendable feature in a work of this kind. It is a good type of working manual, of the old-fashioned kind, brought up to date, and should retain the popularity of the two former editions. G. M. C.

SURGICAL CLINICS OF CHICAGO. Vol. IV, No. 2, April, 1920. Pp. 222; 79 illustrations. Philadelphia and London: W. B. Saunders Company, 1920.

AGAIN it is the pleasure of the reviewer to say a good word for the *Clinics*. This number, though smaller than the average, is equally as good if not better than some of the preceding volume numbers. The same high standard is maintained in both the contributors and the subject-matter.

The *Clinics* is famous for the variety and interest of the subjects. In fact very often one gets a much more interesting and instructive grasp of a subject read here than he could obtain from a text-book.

The number is full of excellent ideas. E. L. E.

PASTEUR. THE HISTORY OF A MIND. By EMILE DUCLAUX, late member of the Institute of France, Professor at the Sorbonne and Director of the Pasteur Institute. Translated by ERWIN F. SMITH and FLORENCE HEDGES, Pathologists of the U. S. Department of Agriculture. Pp. 363; 35 illustrations. Philadelphia and London: W. B. Saunders Company, 1920.

NOT the least interesting part of this delightful volume is the introduction. Here the translators give the life history of the author, Duclaux-Ducleaux, the pupil and friend of Pasteur, in himself a genius. The first part of the book proper deals with the predecessors and teachers of Pasteur, Hauy, Weiss, Delafosse, Biot and Herschel, and shows how Pasteur acquired the taste for researches of a certain type. Altogether there are eight parts to the book, each divided into its component chapters, and comprising in the main the following subjects: Works on crystallography; lactic and alcoholic fermentations; spontaneous generations; wines and vinegars; studies on the diseases of silkworms; studies on beer; studies on the etiology of microbial diseases and the study of viruses and vaccines. Most interesting are the studies on silkworms.

In these pages, as elsewhere in the book, one may follow the workings of Pasteur's mind, or at least the analysis of thought and motives as elaborated by Duclaux. The study of viruses and vaccines, including the chapters on rabies is absorbing. Throughout one is held by the fact that one receives not only the results of successful research, but the pathways leading to success are mapped out and detailed, and the failures and mistakes of a great intellect are impartially laid bare. A. G. M.

PERSONAL BEAUTY AND RACIAL BETTERMENT. By KNIGHT DUNLAP, professor of Experimental Psychology in the Johns Hopkins University. Pp. 95. St. Louis: C. V. Mosby Company, 1920.

THE author presents for consideration a conception of beauty which differs from that found in poetry, song and romance. Beauty is of importance from the point of view of the race and of civilization. In the detailed character of beauty, stature, bodily proportions, features, hair, fat, muscular tonicity and poise are considered. (Incidentally it may be saddening to the reader to see that lack of the pate-hair is a fatal bar to beauty.) The combination of these characteristics is the expression of the potentiality of the individual and shows what he is capable of doing for the species. The most beautiful woman and the handsomest man are the persons we would choose to be coparents of our children. The procreation of children is considered the predominant ideal in marriage. Human beauty is a sign of fitness for parenthood. The conservation of beauty is the problem of the present day and of all time.

These, in brief, are some of the main points brought out by the author. Prostitution, the effect of war, the stage and other factors are discussed in their relationship to beauty and sex-selection and breeding. A. G. M.

THE OPIUM MONOPOLY. By ELLEN N. LA MOTTE. Pp. 84. New York: The Macmillan Company, 1920.

MISS LA MOTTE'S small book is an interesting statistical study of the opium production and sale in various English colonies. She makes out a rather strong case against the British Government's monopoly and open sale of this insidious drug. A large number of Englishmen recognize the immorality of the opium trade which flourishes under the British flag. The evil is well recognized in England. As such is the case it does not seem to be appropriate for an American to write a diatribe against a trade which is totally English and of which enlightened Englishmen are well aware and against which they have frequently protested. It does not seem

incumbent upon us Americans at any time, and particularly at the present time, to call attention to any moral obliquity which exists in England and her colonies. Nor does it seem that Miss La Motte has presented sufficiently strong evidence against the opium trade to warrant the publication of a book such as this, written by an alien. Furthermore, there are enough evils existing in this country, and no one who has read *The Backwash of War* can fail to appreciate that the author is well able to ferret out and to discover all that is disagreeable, for the correction of which Miss La Motte could apply herself with greater advantage than attempting to judge the turpitude of other nations. J. H. M., JR.

PRINCIPLES OF HUMAN PHYSIOLOGY. By ERNEST H. STARLING, M.D., Jodrell Professor of Physiology, University College, London. Third edition. Pp. 1315; 579 illustrations. Philadelphia: Lea & Febiger, 1920.

THIS third edition of Starling's *Physiology* is generally well balanced in presenting the various phases of the subject from the underlying physical and chemical basis to the outlying topics, which are far-reaching in clinical application. The introduction epitomizes the text in considering the phenomena of living matter as based on adaptations which are reactive "adjustments of internal to external relations." Topical arrangement of the text gives general physiology 164 pages, mechanisms of movement and sensation 462 pages, mechanisms of nutrition 608 pages and reproduction 48.

Characteristic features of marked value are frequent paragraphs on comparative anatomy and physiology, full illustrations by excellent diagrams, notably of nerve pathways and consideration of general physiology. Discussion of practical topics gives evidence of scope and up-to-date character, *e. g.*, defence of the organism against infection, nourishment and protection of the eye, referred pain, spinal shock, speech, voice-production, vitamines, etc. In a masterly manner, both as regards text and illustration, Dr. H. Hartridge revises the section on sense organs, and is entirely responsible for the chapters on vision. But fifty additional pages allotted to vision tend to overbalance other equally important topics. One wonders when it appears first among the senses whether the innovation is to honor the writer or the function. Starling's distinguished investigations in the field of nutritional mechanisms account for the especially scientific presentation of these subjects. He includes latest developments in regard to functions of each system often adding interest with descriptions of methods and apparatus by which experiments are made.

In the preface the author generously asks for suggestions that will make the book more useful. The present reviewer emphatically suggests enlargement of the index by more complete crossing to save time; addition of references to stimulate reading and frequent insertion of dates to vivify the text and add perspective.

Those who already know Starling's *Physiology* are grateful for this splendid revision. New readers, whether students or physicians, will have a treat, for this book is a storehouse of information in regard to fundamental facts and theories with their practical applications presented in most acceptable form. R. W. L.

HANDBOOK OF DISEASES OF THE RECTUM. By LOUIS J. HIRSCHMAN, M.D., F.A.C.S., Detroit College of Medicine. Third edition. Pp. 378; 227 illustrations, 4 in color. St. Louis: C. V. Mosby Company, 1920.

A BOOK written essentially for the general practitioner, yet from the authority of a specialist; a book covering a field of work that every physician meets daily, yet in which he is so often completely at sea; a book detailing the office technic in its simplest, safest and surest form, yet from the knowledge of one with vast experience; outlining the surgical procedure in harassing conditions that are too often treated in a palliative way, yet are in truth easily amenable to cure under a local anesthetic; a book illustrated so copiously that the pictures alone tell all the essential steps, yet with a text that is delightful reading. Such is Hirschman's *Handbook*, and its appearance in its third edition is welcomed. Hirschman states that 75 per cent. of the surgical operations about the anus and lower rectum can be made easy office procedures if one but follows the technic of local anesthesia he gives. The chapter on constipation is excellent. Pruritus, ulcer, fissure, fistula, abscess, hemorrhoids, inflammations and polypi are all splendidly presented. It is a pity that the chapter on dysentery has been entrusted to other hands, for though the subject is covered by an authority its diction is very poor and in places ambiguous. We would suggest, as a minor criticism, that in subsequent editions the chapter on anesthesia be placed nearer the front of the book and so eliminate reiterative reference, and that the various operative methods advised for hemorrhoids be more clearly differentiated in the text. The author need not apologize for his specialty. His book should command the greatest respect and be to anyone a valuable reference volume.

A. R.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

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Habitual Dislocation of the Shoulder.—OLLERENSHAW (*Jour. Orthop. Surg.*, 1920, ii, 255) reports very briefly 4 cases, one of which was operated on before he saw it but nothing is said of the particular operation performed or its results. He did the Clairmont operation on 3 of the cases. This operation provides a muscle flap fashioned from the deltoid which is passed around the head and neck of the humerus and acts as a sling to brace the head and keep it in the socket. All 3 cases were operated on in the past year which does not entitle him to refer to them as permanent successes. He intends to deal with any future cases by this muscle flap operation and at some future date to report on all such cases including those referred to in this paper. He tells of a paper by Armour read before the Liverpool Medical Society in 1914 in which 2 cases operated on by this method were reported. In the first the dislocation recurred a few months later. The second had had no dislocations since the operation. In the discussion which followed Ollerenshaw's paper, Dunn said he had seen a good many operations done for this condition and that in his experience excision of a portion of the capsule or plication of it has not infrequently been followed by recurrence. In one such case Clairmont's muscle flap operation gave a good result. One case upon which he did a Clairmont operation, fifteen months before, recovered completely free motion of the joint and was discharged three months after operation. He has not heard from this patient since. Bristow said that he had done this operation on the right shoulder of an epileptic which had been dislocated eighteen times, the left shoulder having been dislocated sixteen times. The operation had been done six months before and since then he had several fits and dislocated his left shoulder four times but the right had not since come out. Since then he has operated on the left shoulder as well. He attributes the good results of the operation to the big lump of ragged muscle placed under the capsule strengthening the part and to the effect of the hemor-

rhage which leads to the formation of fibrous tissue. He is not inclined to give much credit to the special action of the transplanted slip of muscle. Platt did this operation five years before on a professional acrobat and no dislocations followed the operation, but he had lost so much deltoid that his shoulder-joint musculature was incapable of bearing the full brunt of his gymnastic maneuvers. He entered the army, but Platt believed in a comparatively low category. Threthowan plicated the capsule in 2 cases, in 1 twelve months and in the other fifteen months before, and he had not heard that they had relapsed since.

Pseudomyxoma Peritonei.—Biggs (*Ann. Surg.*, 1920, lxxi, 619) says that this condition may be described as an inflammation or irritation of the peritoneum, caused by the discharge of the epithelial lining and the contents of a pseudomyxomatous cyst of the ovary or appendix, and resulting in the production of pseudomucin and secondary tumor formation. He thinks that the most tenable theory as to etiology is that of cellular implantation: the epithelial cells lining the cyst, together with the pseudomucinous content of the cyst, being discharged through a rupture of the cyst wall into the peritoneal cavity, the cells there functioning as they did in their original situation. Five cases are reported with the operative and pathological reports in each. He concludes that the condition is much more common than is generally recognized. Caused by cellular implantation it is histologically benign, but may be clinically malignant. If it is considered to be a form of cancer, it must be assumed that pseudomucin inhibits its destructive power. It may originate in the ovary or the intestinal tract; ovarian origin being by far the most frequent. If it is appendiceal in origin, the appendix has been the seat of chronic inflammation. Early invasion of the peritoneum is characterized by a pebbly appearance. In early cases the condition will sometimes be cured, and at any stage it may be inhibited, by operation.

Birth Paralysis.—Platt (*Jour. Orthop. Surg.*, 1920, ii, 273) reviewed the literature in an effort to arrive at a working hypothesis in dealing with these cases and particularly in our teaching. He has had 23 cases of birth paralysis and in analyzing them he makes four groups. In group 1, in which there were 12 cases, the actual paralysis had recovered and the patients presented the typical subluxation of the shoulder-joint with a fixed internal rotation curvature of the arm. The mechanical disablement was due simply to the torsion and the general underdevelopment of the limb in length and caliber according to the length of time the disability had existed. Group 2, in which there were 6 cases, showed a typical subluxation of the shoulder-joint combined with a residual paralysis affecting the extensors of the wrist, fingers and thumb. The paralysis in the extensor group of muscles recovered under postural treatment in 4 out of 6 cases. In group 3 there were 3 cases which showed varying grades of paralysis. In two the paralysis was observed later to have disappeared completely. In group 4 there were

2 cases which showed exceedingly flail limbs. In one the right arm was profoundly wasted as seen in anterior poliomyelitis and there was the usual downward subluxation of the head of the humerus. Platt performed an arthrodesis in this case. In the second patient, a girl of eighteen, the left arm showed profound atrophy and lack of development in the left upper limb with a flail shoulder and wrist-joint. Platt explored the plexus above the clavicle in this case but found no trace of any lesion in the supraclavicular triangle, the nerve cords being intact but small and on stimulation giving results identical with the clinical findings. He experimented on stillborn full-time fetuses, employed all varieties of violence embodying the maneuver of separation of the shoulder from the head both before exposing the plexus and after. He failed to rupture any cord in any experiment, and on the closest inspection was unable to see any evidence of rupture of the nerve sheath. With excessive force he was unable to produce any dislocation of the shoulder-joint, separation of the epiphysis or in fact any demonstrable lesion of the shoulder-joint capsule. After weighing the clinical evidence he concludes that there is a certain amount of evidence in favor of including under the head of birth palsy two distinct groups of lesions. Under treatment he suggests that before the supraclavicular plexus is exposed in a case of birth palsy there should be in addition to complete paralysis of a muscle group which has persisted for more than twelve months, definite wasting such as is seen in true complete nerve injuries.

Compression Fractures of the Lower End of the Radius.—STEVENS (*Ann. Surg.*, 1920, lxxi, 594) says that fractures of the lower end of the radius (so-called Colles) are always compression fractures, the compressive side breaking first, literally collapsing. The first point of fracture is the point of greatest compression upon the cortical surface of bone because the stress increases both in compression and tension the further away from the neutral axis. It breaks in compression because the compression is much greater than the tension. Green bone reacts to strain like wet timber. It breaks at the lower end of the radius because there are several forces, and the resultant is on the lower end of the radius posteriorly. This is due to direct compression from above, the hammer blow from below, the resistance both to compression and to blow being not in the center of gravity, but excentric to it and, therefore, increasing the strain. It is also due in part to the velocity of stress and the molecular inertia of material. The compression fractures of the lower end of the radius show the evidence of compression. There is actual loss of substance but no impaction. Breaking up of the impaction (so-called) cannot restore the planes of the articulation, nor does it do so. It might be possible by traction over a long period of time to separate this crushed surface and permit its being filled in by new bone, thus replacing the planes of the articulation, but to do this would be to sacrifice some of our chances of securing a freely movable joint. Early reduction followed by early passive and active motion will return all or nearly all compressive fractures of the radius to useful light occupation within twenty-days. Any retentive apparatus other than a leather wrist strap after ten to twelve days is contra-indicated except in a very rare instance.

Finger Exploration of Gunshot Wounds of the Brain.—Towne and Goethals (*Ann. Surg.*, 1920, lxxi, 531), from a careful study of 28 cases and of the literature, concluded that the entry of a foreign body into brain tissue causes irreparable damage to a more extensive area than that involved in the actual tract of the foreign body, and this cavity is further broadened by hemorrhage; hence the size of the metallic fragment or of the dural aperture is not a true index to the wider area of damage represented by the brain cavity. When such a cavity is not over 7 cm. deep and large enough to admit a finger, cleaning with forceps under careful finger control gives absolute insurances against sepsis, and only very rarely causes increased cerebral trauma which is slight and recoverable. Cleansing of such a cavity by Cushing's method of catheter palpation is sometimes not complete and therefore does not always prevent sepsis; it necessitates a prolonged operation; and it is successful only in the hands of those who have had a large experience in its technic. Brain wounds not suitable for finger palpation must be cleaned as well as possible by the catheter method, curettage, or magnet extraction, or a combination of these methods. The tendency of the difficult catheter technic to make this a special field, which requires that the wounded undergo delay if a trained neurological surgeon is not at hand, is not for the best interests of the patient, who is put under increasing risk of encephalitis with every preoperative hour. Brain wounds, and especially those suitable for finger palpation, are easy to clean rapidly and successfully if a few proper instruments are available. Any surgeon fitted to do front line work can quickly acquire the technic and do these cases in well under an hour; and, with experience in judging which casualties are inoperable may well succeed in evacuating 75 per cent. or more of his operated cases.

THERAPEUTICS

UNDER THE CHARGE OF

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The Effect of the Subcutaneous Injection of Adrenalin Chloride on the Heat Production, Blood-pressure and Pulse-rate in Man.—In a series of 73 experiments on patients suffering from various disorders of the ductless glands, Sandiford (*Am. Jour. Physiol.*, 1920, li, 407) found that adrenalin chloride (0.5 c.c. of 1 to 1000) injected subcutaneously invariably caused an increase in the metabolic rate, usually accompanied by an increase in ventilation and respiration rates, number of heart-beats per minute, volume of each beat and a greater utilization

of the blood-carrying power and peripheral dilatation, with an increased systolic and decreased diastolic blood-pressure. No relationship was found between the intensity of the adrenalin reaction and the degree of hyper- or hypothyroidism. The author found a metabolic rate curve following the injection of adrenalin similar to that found by Lusk from a carbohydrate plethora, and suggests the possibility that the increased heat production is due to an excess of carbohydrate metabolites. In addition there may be a direct stimulation of cellular combustion.

The Results of Protective Inoculation Against Influenza in the Army at Home, 1918–1919.—LEISHMAN (*British Med. Jour.*, February 14, 1920, p. 214). The vaccine formula recommended by a conference of bacteriologists, of which Leishman was chairman, was as follows: B. influenzæ, 60 millions; streptococci, 80 millions; pneumococci, 200 millions per c.c. Several strains of each organism were used. Two doses were given, the first 0.5 c.c., and the second, after ten days' interval 1 c.c. The following table is a summary of the results obtained:

	Inoculated.	Non-inoculated.
Number	15,624	43,520
Incidence of attack per 1000	14.1	47.3
Incidence of pulmonary complications per 1000	1.6	13.3
Deaths per 1000	0.12	2.25

Later, as the etiological role of Pfeiffer's bacillus came more and more into prominence, the vaccine formula was revised so that each cubic centimeter of the vaccine now in use contains 400 millions of B. influenzæ.

Intravenous Protein Therapy.—The principal "foreign proteins" employed intravenously by Gow (*British Med. Jour.*, February 28, 1920, p. 284) are peptone and emulsions of the coli-typhoid group of organisms, the protein-complex of this group being the most efficacious in inducing the "protein shock." He has also used autogenous vaccines in pyelonephritis with good results. Within fairly wide limits the size of the dose of killed B. coli vaccine has little effect on the severity of the reaction. The initial dose may be between 50 and 100 millions. The reaction induced by peptone is proportional to the dose; he gives from 5 to 10 c.c. of a 10 per cent. solution. He describes in detail the technic of administration and the reaction of the patient: rigor, abdominal distress, fever, drop in blood-pressure, decrease in the number of the white blood cells followed by a rapid increase to a maximum of 20,000 to 30,000 per c.c. There may be dyspnea and cyanosis, which are speedily relieved by the hypodermic injection of adrenalin of atropine sulphate. Usually most of the symptoms have subsided by the seventh hour, the temperature returns to normal within twenty-four hours; occasionally facial herpes develops two or three days later. The principal types of cases benefited are: Infective diseases in which the infective organism is known and in which the vaccine is given for specific and "shock" effect. Those in which the causal organism is unknown

(rheumatic fever, etc.). Here the protein treatment is given solely for its non-specific effect. Those in which the causal organism is known (pneumonia, gonorrheal arthritis, etc.), but in which specific vaccine therapy is of little value. Here, too, the vaccine is given entirely for the shock effect. Chronic disorders of doubtful or unknown etiology (psoriasis, bronchial asthma, etc.). In pyogenic affections, both local and general, intravenous vaccine therapy is of value. In septicemia it is difficult to produce a rigor with a plain or sensitized vaccine alone. As the ultimate results are better when such a reaction occurs, Gow recommends the simultaneous subcutaneous administration of anti-streptococcus pyogenes serum. This renders the reaction more likely to ensue, possibly owing to the more rapid liberation of endotoxin. He has given peptone intravenously in conjunction with sensitized vaccine subcutaneously in streptococcal septicemia, and is convinced of its beneficial effects. In conclusion, Gow states emphatically that even in those diseases in which it is of value, intravenous protein therapy is to be regarded solely as an accessory to other remedies.

Anemias of the Hemolytic Group.—WARD (*Proc. Roy. Soc. Med.*, 1919, xiii, Sec. Med., p. 1) believes that there is a group of anemia, or of morbid states without anemia characterized by (1) familial, hereditary or any congenital tendency; (2) paroxysmal course; (3) changes in erythrocytes; (4) due to changes in plasma; (5) tending to make red blood cells more easily destroyed. The diseases, with the exception of hemolytic jaundice, are rare. They are (1) congenital hemolytic jaundice; (2) Dresbach's syndrome; (3) Herrick's anemia; (4) Malin's syndrome; (5) Clough and Richter's syndrome. (I) Hemolytic jaundice, as is well known, is either familial, hereditary or congenital. The acquired type differs somewhat but is more like the familial type than any other disease. Paroxysms of hemolysis are usually observed. The erythrocytes are more fragile than normal and there is an abnormal number of reticulated cells. No absolute proof of plasma changes has been demonstrated. (II) Dresbach's syndrome consists of the presence of elliptical erythrocytes in a healthy man. Three such instances are known. There is no anemia. Bishop's two cases were children of the same family. (III) Herrick's anemia, the so-called "sickle-cell" anemia, has occasionally been familial in occurrence. The course is paroxysmal with acholuric jaundice. The plasma of some of these cases produced similar changes in the red blood cells of the father's blood. All the patients were negroes or mulattoes. (IV) Malin's Syndrome: The characteristic feature is anemia with splenomegaly and the presence in the blood of active phagocytes. Only three cases are on record. The white blood cells increase in number and the red blood cells decrease in number, with progressive splenic enlargement. The relation to leukemia is not known. Both red blood cells and white blood cells are devoured by the phagocytes. (V) Familial auto-agglutination was described by Clough and Richter occurring in a mother and daughter. No other evidence of hemopoietic disease was present. Group Pathology: There is a primary disturbance of the plasma, which may alter the reaction of the red blood cells to hemolysis or change their shape or alter their humoral reactions in some unexplained way, thus allowing auto-agglutination or phagocytosis.

Tuberculous Empyema. — DUHOFF (*Am. Rev. Tuberculosis*, 1919, iii, 590) reports on 20 cases of tuberculous empyema observed among 902 patients (2.2 per cent.). Among these patients 48 were treated by artificial pneumothorax and 10 of these developed a tuberculous empyema. The onset is usually sudden, due to rupture of the lung. The temperature rises and there is pain and dyspnea which lessen as the effusion appears. Symptoms of toxemia and fever may be strikingly absent for many months. There is usually a well-marked pulmonary lesion. Dyspnea is usually absent after the initial reaction. The condition may be latent for years. In this series four ruptured into a bronchus and six burst through the chest wall. Diagnosis depends on study of the pleural fluid in which B. tuberculosis is usually easily demonstrable. At times acid-fast bacilli are found although guinea-pigs are not infected. Prognosis is bad but duration of life depends on the amount of pulmonary involvement and on the presence of complications as well as on the patient's resistance. Treatment: The author has tried many kinds but thinks the patients do better when let alone, unless there are reasons for relieving pressure symptoms. Thoracentesis may often be followed by a persistent sinus. When symptoms are marked and there are rapid cachexia, high fever, etc., rib resection and drainage offer the only chance of prolonging the patient's life. The author states that the fluid is pus or seropus, due to infection of the pleural cavity by B. tuberculosis, caused usually by lung rupture often following artificial pneumothorax.

A Preliminary Study of Clinical Activity.—BROWN, HEISE, PETROFF and SAMPSON (*Am. Rev. Tuberculosis*, 1919, iii, 612) attempt to define clinical activity as that state in pulmonary tuberculosis in which pathological activity is not latent but is producing through the actual and immediate absorption of poisons certain clinical or laboratory manifestations of disease, which disease may in turn be progressing, stationary or even for the time-being retrogressing. If tubercle bacilli are present in the sputum, clinical activity is three times as likely to occur if rales are present, but even then only one-half of these are clinically active. If tubercle bacilli are not present, then clinical activity occurs in only one-fifth of the cases irrespective of whether rales are present or not. In cases without rales as many patients are clinically active when tubercle bacilli are absent as when present. In eleven (44 per cent.) of the 25 cases without tubercle bacilli only a peribronchial or questionable parenchymatous lesion was found. Of these 11 cases, 6 had hemoptysis, 1 had tuberculosis of the eye and 4 had pleurisy. As far as could be ascertained clinical activity does not vary whether sputum is present or absent. Whether rales are present or absent in patients with or without sputum is also of no importance.

Concerning Sensory Localization in the Cortex.—La question des localisations sensitives de l'écorce et le syndrome sensitif cortical. PIERON (*Rev. de méd.*, 1919, xxxvi, 129) has very thoroughly reviewed the literature concerning sensory disturbances following cortical lesions and has abstracted 21 cases and presented 3 new cases. The case records and

discussion of earlier views may be read by those interested in the subject. The author concludes: "The war wounds have shown that the sensory areas of the body are in the post-central gyrus and that all types of sensation are thus represented in a very small area. Distinct topography of the post- and preaxial halves of the extremities is present. The perceptive functions, dependent on associative phenomena in the sensory cortex, are very easily disturbed by diffuse lesions. Varous modalities of sensation are more easily disturbed than others, dependent somewhat on the nature of the lesion. In grave lesions the anesthesia may be complete. In less extensive lesions the sense of position and movement is usually more disturbed than the other modalities of sensation, although these too are often altered in varying degree. There is thus no pathognomonic dissociation of sensation due to cortical lesions, although the syndrome of Verger-Déjerine is the most constant. The syndrome thalamique differs from the cortical syndrome, if viewed only from the sensory standpoint, by the different behavior of the sense of pain and by the affective reaction of the patient, produced by the sensory changes."

Meningococcemia Without Early Meningeal Involvement.—Ribierre Hérbert et Bloch (*Ann. de méd.*, 1919, vi, 341). The authors report 5 instances of prolonged intermittent fever in which the meningococcus was grown from the blood and 2 other cases not proved bacteriologically but probably belonging to this group. The symptomatology varied markedly. The fever, as a rule, is intermittent, with frequent chills, at times resembling charts of malaria patients. Eruptions, usually of papulo-erythematous type, are common. Usually a few new spots occur after a high rise in temperature. They may appear on any part of the body but are most frequent on extensor surfaces of knee and elbow and on forehead. Arthralgias and myalgias are as frequent as fever and efflorescence. The commoner joints affected are knee, elbow and ankle. The joints often become red, swollen and tender. Persistent myalgia is not infrequent. Most observed cases of meningococcus septicemia have terminated by meningeal involvement. Three of these cases presented meningeal involvement after the first, second and third months respectively. In some of the cases the cerebrospinal fluid showed increased cells and globulin, which, however, disappeared quickly when small doses of serum were injected. In 1 case an endocarditis of the aortic valves developed which was due to the meiningococcus and quickly terminated fatally. The duration of the disease varied from fifty to one hundred and thirty days. The general condition of the patient remained good, as a rule, in spite of the high fever. Cultures of blood should be made in ascetic bouillon or egg bouillon. In 2 instances the organism was agglutinated by antimeningococcus serum and in 3 instances by antiparameningococcus serum. The cases were treated, as a rule, by specific antisera in large doses, both subcutaneously and intramuscularly. Two of the cases died. One of endocarditis and one during a chill.

PEDIATRICS

UNDER THE CHARGE OF

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Gonorrheal Infection in Childhood.—BLAND (*New York Med. Jour.*, March 20, 1920) points out that gonorrheal infection in little girls is extremely common, but it is obviously impossible even to guess how frequently this disease really occurs. Guiteras considers that 75 per cent. of the cases of vulvovaginitis is due to gonorrheal infection. Saprophytic organisms cause the remaining 25 per cent. of cases. In the great majority of the cases of vulvovaginitis the infection is indirect and is often conveyed through ignorance or carelessness. The forms and methods of conveyance are innumerable. The clinical thermometer is said to form a common medium of transfer. Underclothing, bed linen, napkins, towels, sponges, wash cloths, syringes, bath tubs, and even bath water may be the medium of contamination. The majority of cases occur in early life usually between the second and tenth years. In most cases the systemic and local symptoms of vulvovaginitis are moderate and the course of the disease is also relatively mild. The constitutional reaction to the disease is not commonly observed by the physician as they have usually disappeared by the time that the patient appears for treatment. The child usually complains of itching. There is also burning and stinging which is usually aggravated by urination. This may cause a voluntary retention of urine. Shortly after the onset of the disease the discharge appears. At first it is thin and ichorous; later it becomes thick, yellow or yellowish green, and profuse. In the still later stages it becomes mucoid, creamy or watery. The diagnosis should be made first by a careful analysis of the clinical history, second by painstaking physical examination, third by a microscopic examination of the discharge, and fourth by a serological or complement-fixation test. In the treatment prevention should be emphasized. This is especially imperative in institutions. In the prophylaxis the most important point is the examination of the vulvovaginal secretions of all female children. When the disease appears isolation is most important. This should include instruments, linens and utensils as well a physical isolation of the individual or individuals. The author begins active treatment gently so as not to upset the small patients. His first step is irrigation with a non-irritating solution such as boric solution or preferably sterile water. After the confidence of the child is gained he employs Lugol's iodine solution in warm water. The solutions are applied through a number four soft rubber catheter. He begins with a weak solution, usually a quarter of a teaspoonful to 2 quarts of water or about a quarter of 1 per cent. solution. This is gradually increased until the strength reaches 1 per cent. Not less than one gallon of solution is used at a sitting. This is done morning and evening for three or four weeks. Once a day about 15 minims of a 25 per cent. solution of argyrol is instilled into the vagina with a medicine dropper.

At the same time the vulva is painted with the same solution and a pad of cotton saturated with the same is applied to the labia and vestibule. After four to six weeks the irrigation is used only once a day. Treatment is continued until four successive negative smears are obtained and until the complement-fixation test is negative.

Prognosis in Operated Cases of Hypertrophic Stenosis of the Pylorus.—GOLDBLOOM and SPENCE (*Am. Jour. Dis. Children*, April, 1920) base their report on a study of 163 cases operated by the Rammstedt method during a four-year period. They found that the duration of symptoms prior to operation was probably the most important single factor affecting the prognosis. When symptoms had lasted less than four weeks the mortality was one-third as great as when they had lasted four weeks or longer. The mortality-rate in artificially-fed babies was more than three times that for breast-fed babies. In infants weighing seven pounds or less the mortality was three and a half times greater than in those whose weight exceeded seven pounds. The mortality increased in direct proportion to the amount of weight lost previous to operation. The mortality for breast-fed infants who had vomited for less than four weeks, and who had lost less than 20 per cent. of their best weight, was almost nil. The fatalities which occur are due to accidents which are avoidable when the operation is done by a skilful surgeon.

The Clinical Role of the Fat-soluble Vitamin: Its Relation to Rickets.—HESS AND UNGER (*Jour. Am. Med. Assn.*, January 24, 1920) say that it would lead too far away from the subject to discuss the various theories that have been advanced to account for the occurrence of rickets, and as the data are not adequate no definite conclusion can be made. There seem to be several causes at work, rendering the unravelling of the problem so difficult that there is a difference of opinion not only as to the particular dietary factor that is at fault, but even as to whether rickets is to be considered a disorder of dietetic origin. It should not be lost sight of that there is a prenatal factor involved. The fact that the negro infant, living side by side with the white in the larger cities and obtaining milk from the same source, develops rickets so frequently and so markedly, indicates that there are important influences to be reckoned with in addition to the food. In considering the diet a most important question is whether the recent theory as to the vitamin origin of this disorder can be maintained, and, more particularly, whether rickets should be attributed to a lack of the fat-soluble vitamin. The clearest understanding of this aspect can be obtained by comparing this disease to the well recognized and established deficiency diseases, scurvy and beriberi. By comparison it is shown that these two disorders are commonly manifested by weakness and inanition, and there are not the fat apparently healthy babies seen in rickets. The most important thing is the fact that neither can be brought about by overfeeding. Rickets frequently develops in infants, receiving too much milk rich in fat, proteins and salts. It is impossible to make this fact go with the thought of a deficiency disease. The studies of the authors show that the fat-soluble vitamin is not the controlling influence. They also show that infants develop rickets while receiving a full amount of this principle, and that they do mani-

fest signs, although deprived of this vitamin for many months, and at the most vulnerable period of their life. They do not find it possible to accept the term "fat-soluble vitamin" as synonymous with "anti-rachitic factor." They say that the danger to infants of a diet deficient in fat-soluble vitamin is slight, provided it contains a sufficient amount of calories and is complete in other ways. The infants can maintain their health and vigor in spite of taking in amounts of fat-soluble vitamins so small that they are rarely encountered in ordinary times. In spite of the fact that this vitamin is not widely distributed in nature, a disorder that may be termed "fat-soluble deficiency"—marasmus or xeropthalmia—is hardly to be appreciated from a clinical standpoint. The study of rickets was undertaken on 100 children in a modern child-caring institution. These infants lived under excellent hygienic conditions, their nursing and care was the same, their food was prepared in a central diet kitchen, and they remained in the institution for the entire period of observation. Once a month they were examined for rickets. This included a notation as to the size of the fontanelle, the beading of the ribs, the enlargement of the epiphyses, the condition of the musculature, the eruption of the teeth, the static development and the like. They were placed on various diets; an abundance of fat and fat-soluble vitamin in the form of milk and cream, a deficiency of these substances as in skimmed milk, and abundance of water-soluble vitamin as in autolyzed yeast, and diets such as Mellin's food or condensed milk. In all cases there was but one deficiency in the diet, which was adequate in quantity and therefore in its caloric value, and contained in every case sufficient antiscorbutic foodstuff. They realize that a test of this kind should be carried out for years and consequently it is impossible to lay down absolute conclusions. They were able to draw some conclusions. They call attention to the fact that the laboratory results are absolutely at variance with the opinions of most clinical observers, who believe that rickets follow overfeeding. There is no delicate indication of what may be termed latent rickets or subacute rickets. This can only be recognized by matabolism tests. After a preliminary study they found that beading of the ribs, especially in conjunction with the enlargement of the epiphyses, furnished the most reliable criterion of the course of the disease. It was found that six grades of beading could be distinguished. Physicians in general and pediatricians in particular, regard beading of the ribs as a pathognomonic sign of rickets. The writers noted that there was also a marked beading in infantile scurvy, but that the beading became rapidly less or disappeared upon the administration of orange-juice or other antiscorbutic food. In other words there is not only a rachitic beading but also a scorbutic beading. This conforms to the observation in experimental scurvy, as was noted in tests on guinea-pigs. In the same way but to a less extent in scurvy as well as in rickets there is seen the enlargement of the epiphyses. This is the probable reason of the confusion existing in regard to these two conditions, so that years ago scurvy was thought to be acute rickets. Beading of the ribs may also come about by lack of the water-soluble vitamin. It is of interest to note that beading of ribs has been observed postmortem in cases of infantile beriberi. As regards the influence of hygienic and non-dietetic measures on the development of rickets, it was found that rickets could develop in spite of an abundance of fresh

air. It was also found that a liberal allowance of light could not prevent the development of this disorder. Five children were given daily treatments with the violet ray. This treatment made no improvement on the rickets. The test diets were interesting from a point of view apart from the subject of rickets. In spite of the results of the experiments of others on rats, the authors failed to note similar results clinically. The only abnormal condition that they have noted has been a mild retardation in weight. Their experience led them to believe that under exceptional circumstances as in time of war, the danger to the infant from a deficiency of the fat-soluble factor is one not to cause great apprehension. It is not so widely distributed in nature as the water-soluble vitamin, but infants seem to be able to thrive for long periods on small quantities if the diet is otherwise complete. The great danger arises from diets composed merely of cereals and water or perhaps an insufficient amount of buttermilk or skimmed milk. There is a great danger of attributing to vitamins many little understood phenomena. They call attention to the peculiar and almost specific role played by cereal in the nutrition of infants. The gains produced could be recognized as due to an addition of any of the recognized vitamins, as diets rich in the fat-soluble, water-soluble vitamins, antiscorbutics, were improved by the addition of cereals. It was also not due to the simple increase of caloric value for the amount of food was comparatively insignificant The simplest and most direct explanation of this is that this carbohydrate brings about a more complete oxidation and therefore a better utilization of the food.

OBSTETRICS

UNDER THE CHARGE OF

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The Care of the Pregnant and Nursing Woman.—Bouret (*Arch. mens. d'obst.*, August, 1919) describes methods for caring for pregnant and parturient women in recently constructed maternities and under conditions in which much can be done to improve the health and vigor of the offspring. He believes that a modern maternity should include a portion devoted to the disorders of pregnancy, another in which labor and the puerperal period receive attention and an infirmary for abnormal cases, and in addition an out-patient or dispensary service. The portion allotted to the disorders of pregnancy may contain four rooms, in which are two beds each. The maternity portion for labor and the puerperal period should have twenty beds, of which six are in isolated rooms; twelve in two wards containing six beds each and two beds in a large room with an incubator for infants. The infirmary should have a dozen beds, six in rooms of one or two beds each for infected cases and six for aseptic cases. The dispensary should be connected with the whole of

the maternity. The infirmary department and that devoted to labor should be independent and the infirmary should again be divided into two parts: one for septic and the other for aseptic cases. These should be separated. The infirmary should be of two parts: one for septic and the other for aseptic cases, completely separated, each with its sterilizing room and operating room. There should be independent entrances to this portion of the maternity, but it should be possible to communicate directly with the maternity. While we may condemn such a communication principle, practically it seems very necessary. The maternity proper, so-called, should contain not only beds for the lying-in patients, but rooms devoted to the care of infants and a pavilion for operations. The part reserved for operations is practically a small independent hospital, isolated in such a manner that if necessary one can readily exclude those from without. There should be a sterilizing room, with two large horizontal autoclaves, and not only should dressings be sterilized, but also bed-linen and the garments worn by patients in bed. There should also be two large reservoirs of sterilized water, apparatus for sterilizing instruments, appliances and room for ordinary labor, one for minor obstetrical operations and a large hall for clinics and operations. In each of the operating rooms there should be a copious supply of sterilized water, hot and cold. The sterilizing service of the infirmary should be completely independent of that in the maternity. It may be built on the same model, but it needs to be very much smaller. The writer adds illustrative cases showing the benefits for patients or the different functions of the maternity hospital.

Intra- and Extra-uterine Pregnancy.—BISSELL (*Am. Jour. Obst.*, December, 1919) records the case of a woman, married four years, without children. She had one abortion three years previously. She was taken subsequently with the classical symptoms of ectopic gestation in the right tube. At operation there was a typical ruptured ectopic pregnancy in the right tube. The pelvic cavity was filled with blood-clots, but there was no active bleeding. The tube, ovary and clot were adherent to the uterus and pelvic floor and the ovary and the tube were removed. The left tube and the ovary were slightly adherent. The uterus was large and soft, apparently two months pregnant. The patient made an uninterrupted recovery, left the hospital and returned at the normal termination of pregnancy, when she was delivered of a female child, weighing four and three-fourths pounds. Mother and child made a good recovery. From the interval of time elapsing between the operation and childbirth the question arises as to whether this was not a case of twin pregnancy. Many operators are accustomed to dilate and curette the uterus before removing by abdominal section an ectopic pregnancy. Recent study, however, has shown that this is injurious and the majority of operators omit it.

An Early Ovum in Situ in the Act of Aborting.—WILLIAMS (*Am. Jour. Obst.*, September, 1919) describes a rare and interesting case in which an impregnated ovum was in the act of aborting. The growth of the ovum was thirty-eight days after the end of the last period. The ovum was already abnormal and shows the youngest stage of hydatid mole which the writer has yet seen. The specimen was contained in a

uterus removed by supravaginal amputation from a patient, aged thirty-nine years, married seventeen years, with three children. She had had eclampsia and phlebitis, then double femoral phlebitis, removal of the thyroid and repeated and prolonged attacks of mental depression. When first seen examination showed the uterus the size of a three months' pregnancy, but so firm and hard that a diagnosis of myoma was made. In view of the circumstances of the case it was decided after consultation to perform hysterectomy. This was done by the supravaginal method, retaining the normal tubes and ovaries. A typical corpus luteum was present in the left ovary. The patient's convalescence was uneventful, but her mental condition had not much improved. After suitable preparation serial sections were made of the specimen and thoroughly studied. No trace of the embryo could be found and the conditions were difficult to interpret. The decidua vera was thickest in the midline of the posterior wall. Section through the decidua showed the typical histological structure. The ovum was normal in location, and the only abnormality was the absence of fetal vessels and the parenchymatous stroma of the villi and the presence of large hemorrhagic areas scattered through the decidua outside the area of implantation. The ovum was evidently a very early one and abortion was in progress. One pole of the decidua capsularis had ruptured and the corresponding pole of the ovum was retarded through the defect.

The Pelvic Articulations during Pregnancy, Labor and Puerperal State.—LYNCH (*Am. Jour. Obst.*, September, 1919) reviews the literature of the subject and states that sufficient examples of pelvic separation have been reported to excite interest in its mechanism. It is admitted that both the symphysis and sacro-iliac joints are lined with synovial membrane, and it has been shown that the sacrum normally rotates within small limits on the transverse diameter. The posture of the body is all-important in bringing about these different rotations. When the patient is squatting the promontory of the sacrum is shoved forward and the coccyx backward, thus increasing the diameter of the outlet. When the body is standing weight against the promontory pushes it backward, thus increasing the length of the conjugate vera. As the pelvic joints are softened in pregnancy the movements of the sacrum are increased. This condition consists in the phenomena of labor. Nature uses this condition to assist in fitting the fetus into the pelvis as a preparation for labor. Mercurio's position, afterward described by Walcher, is based upon the rotation upon the pelvic joints. In 500 cases the pelvis had been found more mobile than that of nonpregnant in all but 2 per cent. The separation of the pubis was not more than 3 mm., and only in 16 per cent. was it more than 1 mm. There were symptoms of the condition in 15 per cent. and in 70 per cent. there was change in the gait of the patient. The writer had used the roentgen ray and had studied these joint conditions, and also had an opportunity of observing a case of rupture of the symphysis during labor, the case coming under his observation three years after the rupture occurred. Litzenberg had found in 1000 cases 96 patients who needed treatment because of some abnormal condition of the sacro-iliac joints.

Legislation Against Maternal and Infant Mortality.—FOOTE (*Am. Jour. Obst.*, November, 1919) has gone over the laws enacted by different States to protect mothers and the offspring at the time of birth. The States differ very gently. The New York code is probably the most complete regulation for obstetric practice available. Some of the States attempt to define normal and abnormal cases. In regulating the practice of midwives States differ greatly in the minuteness with which the functions of the midwife are set forth. In several States the treatment of the newborn is described in detail. The majority of States require the registration of births and many exact the registration of the midwife. There is great difference in the standards of medical education to secure a license to practice for both physician and nurses. In some States a certificate of character is required, in some reference from an obstetrical school of recognition, while others conduct examination in various ways. Examination for license to practice include a considerable number of questions in obstetrics. Examination for license is frequently written and oral according with the wishes of the examiners. The penalty for violation of the laws pertaining to parturition differs greatly in different States, and in some fine and imprisonment may be imposed at the same time. Whenever midwives are kept and intelligently supervised the question of disinfection of clothing and equipment is included. Births must be reported in the majority of States within five days after the birth of the child. In summing up the whole situation it is found there is no uniformity of laws or even of required standards. Educational centers should be established to educate women in obstetric practice, whether as midwives, nurses, hospital officials or physicians. Community centers even in rural districts, should prove valuable. Supervisors, suitably compensated, and well-paid obstetrical visiting nurses should be employed as educators of midwives and of parturient women as well.

Extraperitoneal Tumor Complicating Pregnancy.—VAN HOOSEN (*Surg., Gynec. and Obst.*, August, 1919) reports the case of a primipara, aged thirty-three years, who summoned her physician because she was suffering from severe pain. On examination a large mass was found in the posterior cul-de-sac about the size of a very large orange. It seemed to be an incarcerated tube. As the patient was not at the period of viability, she was kept in bed and given narcotics and placed in the knee-chest posture at frequent intervals. By this means she was carried along until the seventh month, when section was performed. On opening the abdomen the tumor was extraperitoneal. The abdomen was closed without performing section. An incision was then made in the posterior vaginal wall and the tumor was found feeling somewhat like a fibroid. While an effort was made to loosen the capsule the tumor was penetrated and was found smooth to the touch and filled with a bran-like tissue. This was freely evacuated, followed by severe hemorrhage, which was controlled by gauze packing. The gauze was removed on the fourth day. On the following day the patient expelled a male child through the vagina. This had been dead for a day or two because the external skin was separating. The mother did not have a high leukocyte count, nor at any time did she have a very low one. She died two weeks after the birth of the child. Ries studied this case and stated that the tumor

which he saw looked like a blood clot. On microscopic examination an enormous quantity of syncytial tissue was found. The gross appearance of the tissue resembled that of a blood-clot. The tumor was undoubtedly a syncytioma malignum.

GYNECOLOGY

UNDER THE CHARGE OF

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Small Radium Dosage in Cancer. — During the past two years SAMUEL (*Am. Jour. Roentgenology*, 1920, vii, 42) has limited his exposures to radium for malignancy of the uterus, to twelve hours, not using over 50 milligrams of the element, the dosage being 600 mg. hours for each treatment. His first year of radiotherapy was very disastrous during which time he used 150 mg. of the element for twelve hours and in a few cases for a longer time Seeing the marked benefit from the smaller dosage, he thought larger doses and heavier screening would accomplish better results, but after seeing quite a number of fatalities which he felt sure were due to overdosage, he now makes the plea for *smaller* doses and at least a ten-day interval between exposures, filtering more at each exposure and stopping for four weeks at the end of the third exposure He has been able to accomplish just as good results with this method as he did with the larger dosage, and with more comfort to the patient The patients are not toxic after the smaller dosage, the bladder symptoms are eliminated and no proctitis is seen, all of which make the patient more miserable than does the growth. He generally gives three cycles of three treatments each with four weeks' rest after each cycle. At the end of three months, the treatments are resumed.

Trichomonas Vaginalis Vaginitis.—A type of vaginitis due to the trichomonas vaginalis, an infusorial animalcule, has been described by DE LEE (*Illinois Med. Jour.*, 1920, xxxvii, 186), which is characterized clinically by obstinate vaginal discharge, pruritus, sleeplessness, burning and general weakness. The vulva and vagina are reddened and often rough like a nutmeg grater and sometimes minute hemorrhages are seen in the vaginal epithelium. The cervix is sometimes affected. The discharge is profuse, mucopurulent, thin, bubbly, acrid and has a disagreeable odor. Its irritating character is shown by the erosion of the skin, and especially in fat women there is an obstinate foul smelling intertrigo. Sometimes there are pointed condylomata similar to those

which are frequently present in cases of gonorrheal vaginitis. The diagnosis is easy. Even the clinical appearance of the vagina will suffice, but it is the work of but a moment to put some of the fresh discharge under the microscope and examine it, unstained, before it dries. The animalculæ are at once discovered by their active flagellation. The treatment that De Lee recommends is also very easy but it must be thoroughly done, preferably by the physician himself. The patient should be put to bed for two days. On the morning of the first day the vagina and vulva are scrubbed vigorously with tincture of green soap and water using a rough cloth and going most thoroughly into every fold and crevice. The soap is then rinsed out with sterile distilled water. This process is repeated three times and then a $\frac{1}{1500}$ bichlorid douche is given with friction, every fold and crevice being washed This is then washed out with sterile distilled water and the patient rests in bed. On the next morning the vagina is again washed out with green soap and water after which it is packed with cotton soaked with glycerine (4 parts) and sodium bicarbonate (1 part). The folds and crevices of the vagina are filled with the cotton and the vulva is smeared with the mixture. Next morning the tampon is removed and a sterile water douche is given. The following morning the secretion is examined under the microscope for trichomonas, but they are usually gone by this time. Only morning and afternoon douches of 2 per cent. soda solution are then given, but if the animalcules should return, the treatment should be repeated.

Rational Treatment of Uterine Cancer.—After reviewing the statistical side of cancer of the uterus, both from the standpoint of operability and of curability, LITTLE (*Minnesota Med.*, 1920, iii, 159) concludes that the rational treatment of carcinoma of the body of the uterus consists of a panhysterectomy followed by prophylactic radiation with radium. In cervical carcinoma in the operable stage, either panhysterectomy followed by radiation or a thorough radiation without operation should be performed. From his present experience and observation, he is inclined to the belief that as good or better results can be obtained from radiation alone, with practically no danger or pain to the patient, radium penetrating beyond where the knife can be used. In inoperable cases, radium is much superior to any other treatment. Where there are large fungating masses producing toxemia, they should be removed with the cautery followed by radiation. He has abandoned the Percy cautery for radium and he does not advocate the Wertheim operation because of its high primary mortality, its serious sequelæ, such as vesical, ureteral and rectal fistulæ, and because there are too few cures to compensate the difficulties and dangers encountered.

Pulmonary Infarction Following Gynecological Operations.—Several consecutive deaths from pulmonary embolism in the Gynecological Department of the Johns Hopkins Hospital aroused the interest of HAMPTON and WHARTON (*Bull. Johns Hopkins Hosp.*, 1920, xxxi, 95). They had been engaged in compiling their statistics but a short while when they made the observation that, in the case of many patients with phlebitis who later developed pulmonary complications, a diagnosis of pleurisy or pneumonia had been made without any reference to the

possibility of infarction. In their clinic the diagnosis of pulmonary infarction has been anything but good. They have recognized only 10 per cent of their cases, which they believe is due to the fact that the diagnosis has been based practically always upon the physical findings in the thorax instead of the whole clinical picture. The typical case of pulmonary infarction occurs in a postoperative patient who is convalescing from a laparotomy, frequently a hysterectomy. This complication occurs practically always in the second or third week after operation. The temperature curve is quite characteristic when not complicated by other factors. The patient has a low unexplained evening temperature of 99° to 100° F. after operation. After the day of the infarction the temperature rises sharply, but seldom goes much above 102° F. The curve is hectic in type, not like that of pneumonia. It reaches its highest point between the second and fourth days and usually drops almost to normal again at the end of a week. Infarction almost always makes its appearance in an acute attack with sharp sticking pain over the ribs as the dominant symptom. The attack may rarely be accompanied by a definite chill, although chilly sensations are rather frequent. The leukocyte count varies between 12,000 and 18,000 and is of little help in the diagnosis. The physical signs rarely make their appearance before the second day and the most constant of these is the friction rub, which was noted in 75 per cent. of their cases. They believe that it is probably present in a greater number, but this represents only those cases in which it was noted upon the history. Rales were heard in 75 per cent. of the cases; they are usually evident a little later than the friction rub. Impairment and changes in the breath sounds appear last and were noted in 63 per cent. of the cases. Pain ushers in the attack and is always the predominant symptum. Cough, while present in 63 per cent. of the cases at some time, is usually not severe, and in most cases is unproductive. Hemoptysis was present in 36 per cent. of the cases and when present, practically clinches the diagnosis. Phlebitis, pain and swelling of the leg occurred in 41 per cent. of this series, and when present is just as confirmatory as hemoptysis. In the typical case, the patient is out of bed, convalescing in a normal way when she is seized with a sharp pain in her side, more especially on deep inspiration. The nurse promptly returns her to bed and takes her temperature, finding it to be 100° F. the ward doctor is informed, makes a careful examination of the chest, but finds nothing definite. The patient is reassured and forgotten. On the following morning, in making his rounds, the doctor is informed that the patient still complains of pain in her side and that her temperature is 102° F. He goes over her chest promptly, finds a friction rub, with a few rales below the angle of the scapula and makes a diagnosis of dry pleurisy. A day or two later the patient may develop hemoptysis or phlebitis of the leg. She usually makes a prompt recovery and in ten days the little pulmonary upset is a thing of the past and forgotten. As a result of their extensive study on this subject, Hampton and Wharton conclude that postoperative venous phlebitis and thrombosis are not peculiar to any particular type of gynecological operations. There are a number of conditions that favor thrombus formation, but they believe that infection and trauma play the most important part. Phlebitis and thrombosis of the leg veins, when associated with pain

and swelling are rarely ever followed by fatal embolism. The important point brought out by this study is that postoperative pulmonary infarction in the majority of cases has heretofore been unrecognized chiefly because too much importance has been attached to negative physical findings and too little reliance placed upon a careful history.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
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The Relation of Pregnancy and Reproduction to Tumor Growth.—While somewhat diverse views have been expressed concerning the influences exerted by pregnancy on tumor growth, the consensus of opinion seems to be that during pregnancy the proliferation of the new-growth is retarded. Obviously experimental animals in which spontaneous tumors develop offer the most favorable opportunity for the exact analysis of the subject. SLYE (*Jour. Cancer Res.*, 1920, v, 25) studied the rate of growth of an alveolar tubular carcinoma of the mammary gland in sixty female mice during their reproductive and non-reproductive periods. All of the animals had previously born young. In thirty of these after the tumor appeared no young were again born and tumor growth in these was compared with that of the remaining thirty, in which young were constantly born after the appearance of tumor. The results tabulated demonstrate in a very striking manner the influence of pregnancy in modifying the rate of growth in the coexistent tumor. The amount of tumor grown by the non-reproducing animals was much greater than that grown by the reproducing animals, the daily rate in the former being much in excess of that in the latter. Tumorous mice which are not bred live from four to six weeks after the appearance of the tumor, which proliferates with great rapidity, while the reproductive animals live from eight months to a year, during which time the tumor becomes almost quiescent. The number of the young borne appears to be a factor in retarding the rate of growth. When the mice cease reproducing the tumors commence to grow again with renewed rapidity and the female only survives six to eight weeks after the birth of the last litter. It was also observed that multiple tumors were more frequent in non-reproducing than in reproducing animals.

The Relation of Inbreeding to Tumor Production.—Since inbreeding does not characterize the human race, any exact and comprehensive data concerning the relation of inbreeding to the incidence and inheritability of tumors must necessarily be derived from experimental animals. Slye has previously demonstrated that cancer inheritance in mice follows Mendelian ratios. These results were obtained by selected

mating. Similarly it is only by selected inbreeding that any increase in the numbers of tumors in a strain can be produced. Thus, SLYE (*Jour. Cancer Res.*, 1920, v, 53), by selected inbreeding (mating brother and sister of a hybrid strain carrying a definite percentage of cancer) in three branches obtained new strains with widely varying cancer incidence. One branch gave a tumor-free line, a second yielded a heterozygous line (*i. e.*, mice not themselves developing cancer but carrying it potentially) while the third was an extracted tumorous line. Since the progenitors of each line were brothers and sisters, and they were bred in the same manner, inbreeding, *per se*, was obviously not a factor in occasioning an increase in cancer. "What is put into a mating, and not the manner of putting it in, determines what characters shall appear in the offspring." It was shown that inbreeding, by lowering the vitality and diminishing the fertility of a strain, could eliminate cancer by racial extermination. It is important, in the analysis of results on the incidence of cancer, either spontaneous or inoculated, to bear in mind that the lowering of the vitality of a strain through inbreeding as well as by the hybridizing of stock which gives rise to inferior and infertile strains tends to decrease the percentage of cancer within the strain. The author maintains that "in the demonstration of the inheritability of cancer and other tumor types in mice their inheritability for man and every other species in which they occur has also been demonstrated." Further, since cancer and non-cancer tendencies segregate out and are transmitted as such in hybrid crosses, cancer being a recessive, can be eliminated from the human race, where the matings are hybridizations, by selected mating.

Varieties of Streptococci with Special Reference to Constancy.—CLAWSON (*Jour. Infect. Dis.*, 1920, xxvi, 93) in a study of strains of streptococci isolated from various sources, paid particular attention to the constancy of the special characteristics, such as peculiarities of morphology, action on the blood-agar plate, fermentation of various carbohydrates, agglutination and complement-fixation reactions, in an attempt to discover whether the various classes adopted by previous workers have sufficient relationship to source, habits, pathogenesis or other particular characteristic to justify such grouping. From the author's investigations there seems to be no direct relationship between the length of chains and pathogenesis in streptococci. Capsules were found less commonly among hemolyzers than among non-hemolyzers. Of the 134 strains, hemolysis was constant after nearly two years of artificial cultivation, only 4 regularly failed to ferment lactose, only 2 always fermented mannit and only 3 always failed to ferment salicin. Evidence pointed to the fact that all non-hemolytic strains were methemoglobin producers when grown on suitable mediums, and of 150 non-hemolytic strains investigated, only 5 always failed to ferment lactose, 36 always fermented mannit and 75 always fermented salicin, there seeming to be more uniformity of fermentation among hemolytic than non-hemolytic streptococci. The regular type of fermentation placed most of the non-hemolytics in the class of S. mitis and S. salivarius (Holman). Considering the lack of relationship between fermentation reactions and source or pathogenesis, and the wide distribution of organisms falling into non-hemolytic groups, the author believes it is

doubtful whether any of the smaller groups of non-hemolytic streptococci deserve a place in classification. He also prefers the term S. hemolyticus to S. pyogenes and S. viridans to S. buccalis (Blake). It was further found that agglutination reaction between hemolytic organism and homologous serum showed a high degree of uniformity, while the reactions of hemolytic serum with non-hemolytic organisms, non-hemolytic serum with hemolytic organisms or non-hemolytic serum with non-hemolytic organisms, except the homologous strains, gave a low percentage of positive results. The reaction of hemolytic serum with hemolytic antigen yielded a higher percentage of complement-fixation than those of hemolytic serum with non-hemolytic antigen, or non-hemolytic serum with non-hemolytic antigen, or non-hemolytic serum with hemolytic antigen. From these observations it is concluded that the hemolytic group is a homogeneous group in which there is a relatively high degree of constancy and that the non-hemolytic group is heterogeneous or less homogeneous than the hemolytic group.

Observations on Paratyphoid Bacilli Recently Isolated from Animals.—In a recent study of the tissues of several hundred swine which died of enteric diseases, SPRAY (*Jour. Infect. Dis.*, 1920, xxvi, 340) found the predominating bacterial flora to be members of the paratyphoid-enteritis group. The materials for study were obtained either from diarrheal swine by routine inoculations from heart blood, lung, liver and spleen, kidney and mesenteric glands, or from hog cholera virus by directly plating or inoculating the virus blood into rabbits. In the case of diarrheal swine the identity of all paratyphoid strains isolated from the various organs of the same carcass was not to be assumed, because in at least three instances, two or even three distinct strains were isolated from the same body. With few exceptions the strains were readily classified. Forty strains were studied in detail by the employment of arabinose, xylose, dulcite, inosite, lead acetate agar, glucose serum water and agglutination and absorption tests; 23 of the forty strains were recovered from the tissues of diseased swine; 8 from hog cholera virus blood by plating and 9 from rabbits dying after inoculation with virus blood known to contain gas-producing bacteria. It was found that 34 of the 40 strains so studied were B. suipestifer, 2 were identical with human B. paratyphosus A, 2 with human B. paratyphosus B and 2 were intermediate between B. suipestifer and B. paratyphosus B. B. enteritidis was not encountered at any time. No true representative of the paratyphoid enteritis group was isolated from the feces nor from the lumen of the intestines. The author emphasizes this as he does the value of the selective cultural media mentioned above.

The Comparative Oxygen Avidity of Normal and Malignant Cells Measured by Their Reducing Powers of Methylene Blue.—An interesting comparison of the reducing power of normal tissue and that of tumors is made by DREW (*British Jour. Exper. Path.*, 1920, i, 115) by means of methylene blue. A measured quantity (0.3 to 0.5 c.c.) of minced tissue was placed in a tube to which was added a definite amount of 0.001 per cent. methylene blue in Locke's solution minus the glucose. In order to prevent reoxidation a layer of paraffin was poured over each tube, which was then incubated at 37° C. During incubation the methylene blue became reduced to methylene white

by the tissue. The reduction commenced in the layer of the solution next the tissue and gradually extended upward in the column of colored fluid. While slight variations in the rate at which the reduction proceeded upward in each tube occurred with individual tissues, a very marked difference was observed between the tubes containing normal and tumor tissue. When the reduction rate was represented by means of a graph, two types of curves, which differed widely from one another, were obtained. In normal tissue the maximum reduction occurred in the first hour and gradually decreased in rate until the fourth hour, when the minimum was reached. The tumor tissues used were mouse carcinoma, mouse sarcoma, rat sarcoma and mammary carcinoma from a human subject. The reduction produced by tissues of these tumors showed a minimum during the first three hours and a small increase in the fourth and fifth hour, when it finally ceased. The only exception among the tumors was a neoplasm containing a considerable quantity of glycogen. In this case the curve tended to approximate that found in normal tissue. The curves obtained with methylene blue could be duplicated when hemoglobin was substituted for the dye, and the author concludes that the difference between the two types of curves is to be explained by the fact that the tumor cells have a lower oxygen avidity than the normal cells.

The Human Fecal Streptococci.—Frequent and fragmentary allusions to the occurrence of streptococci in the gastro-intestinal tract have appeared in the literature. Most studies have had to do with the cause of specific diseases and consequently have presented difficulties of evaluation, often tending to complicate rather than simplify the situation. In an attempt to establish the normal streptococcal flora of the alimentary canal in accordance with the recent methods of classification, OPPENHEIM (*Jour. Infect. Dis.*, 1920, xxvi, 117) examined 55 apparently normal stools from fifteen healthy persons from which 323 strains of streptococci were isolated. The number of samples from any one individual varied from 1 to 5 and the number of strains isolated ranged from 11 to 49. The usual number of samples from one person was 4 and the average number of strains from these 4 was approximately twenty. The method of culture consisted in diluting a few loops of feces in sterile salt solution and streaking the surface of a 10 per cent. sheep blood-agar plate. After eighteen to twenty-four hours' incubation at 37° C. colonies were fished to glucose broth and reincubated. Replatings were made from the broth and the colonies picked to blood-agar slants, from which the carbohydrate media were seeded and read in five days. Meat infusion broth, pH. 7.5, was employed. The carbohydrate medium was 1 per cent. except salicin (0.5 per cent.), and brom-cresol purple served as the indicator. Hemolytic and "indifferent" varieties of streptococci were rarely found. The green-producing strains were most frequently encountered, and of these all fermented glucose, 8 failed to ferment lactose, 9 failed to ferment salicin and 4 failed to ferment mannit. According to Holman's classification, S. fecalis occurred in 73 per cent., S. salivarius in 1 per cent., S. non-hemolyticus I in 23 per cent., S. equinus and S. ignavus in 1.5 per cent. Mannit fermentation, though the most important fermentative characteristic, was found to be quantitatively less uniform than that of

other carbohydrates. No apparent morphologic characteristics aside from those dependent on rapid, luxurious growth, characterized the strains isolated.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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A Study of the Relation of Diet to Pellagra Incidence in Seven Textile-mill Communities of South Carolina in 1916.—GOLDBERGER, WHEELER and SYDENSTRICKER (*Public Health Reports*, 1920, XXXV, 648) set out to determine the explanation for the outstanding fact, observed many years ago, that poor diet was associated with pellagra. Goldberger had earlier called attention to the significance of the fact that nurses and attendants, at institutions where pellagra was rife, appeared to be immune. A study of the conditions showed that the apparently immune used a diet containing less cereal and vegetable components, and more fresh meats, eggs and milk. Experimental studies clearly showed that when the diet of inmates was supplemented so as to contain a larger proportion of animal protein foods the disease disappeared. In one institution the diet of certain patients was supplemented in the manner indicated, while that of others was not changed, with results that clearly proved the prophylactic benefit of the more liberal diet. By feeding a faulty diet to volunteer convicts it was possible to induce pellagra among those, while ten other prisoners remained free. In the present study accurate observations were made on the diet used by pellagrous and non-pellagrous families and on the economic and sanitary circumstances. Special stress was laid on the necessity for data on dietary conditions in the months prior to the annual appearance of pellagra which reaches its height in June. The seven villages were typical cotton-mill communities ranging in population from 500 to 800 inhabitants, practically all of native-born Anglo-Saxon stock. House-to-house visits were made for the purpose of discovering cases that otherwise would have escaped observation; in addition, cases were reported by physicians, though apparently but a small percentage of cases came under medical care. Only cases with a clearly defined eruption were counted as pellagra, though the authors believe that by adhering to this criterion some cases were excluded. The data for basis of the dietary studies were based on records of the purchases or production of food consumed by a household. The outstanding difference between pellagrous households and others lay in the more liberal supply of foods of the animal protein group in the latter. Just what component of these foods is essential in the prevention of pellagra remains to be determined. The results of the study give no support to the theory that

the eating of corn is associated with the development of pellagra. The availability of a more abundant supply of fresh milk and fresh meats is regarded as the most important factor in the prevention of pellagra.

The Diagnosis of Helminthic Diseases of Man.—Hickey, (*U. S. Public Health Reports*, No. 24, 35, 1383) reports on the examination of oriental immigrants at the U. S. Immigration Station, San Francisco, California. The technic employed is as follows: (1) A piece of (preferably) formed stool, approximately the size of a walnut, is placed in a porcelain cup, and after taking about 60 c.c. of cold water, the mass is thoroughly disintegrated with the aid of a wooden tongue depressor. When disintegration of the feces is as complete as possible the tongue depressor is destroyed. If the stool is liquid an equal bulk of cold water is added and mixed as indicated above. (2) After placing over the mouth of the cup two or three layers of wide-mesh surgical gauze, a portion of the contents of the cup is strained into a tube and centrifugalized for ten seconds at 1500 to 2000 r. p. m. The gauze is thrown away and a new piece used for the next specimen. The cup is emptied of its remaining contents and thoroughly scalded. (3) The tube is removed from the centrifuge, and, without disturbing the sediment, the supernatant liquid is poured off and the tube refilled with cold water to about three fourths its capacity. (4) A thoroughly clean rubber pad is placed over the mouth of the tube and held in place by the thumb while the tube is shaken vigorously. When preparing two tubes at the same time extreme care should be taken to use the rubber pads on their respective tubes at each shaking. (5) The contents are again centrifugalized for ten seconds. (6) The supernatant fluid is poured off as described above, the tube is refilled with cold water and again shaken. (7) Centrifugalized again for ten seconds. (8) The supernatant fluid is poured off, leaving about $\frac{1}{2}$ inch overlying the undisturbed sediment. The specimen is now ready for microscopic examination. (9) A smaller amount of the sediment is placed on a slide, and sufficient water is added to almost completely cover it. This is mixed with the aid of a toothpick or match and allowed to stand for two or three minutes; the excess fluid is poured off onto another slide, more water is added and this is allowed to stand while the first slide is being examined microscopically. This procedure can be repeated with a third slide, though usually the second will suffice. It often happens that ova will be found on the second slide and not on the first, on account of the lower density of the former, which permits the ova to settle more readily. With respect to clinical aspects, eosinophilia should always excite suspicion. Anemia may or may not be present and other symptoms may be wanting, even in heavy infestations. The ova of the various parasites, trematodes, cestodes and nematodes are described in detail.

Statistics of Influenza Morbidity.—Frost (*Public Health Reports*, 1920, xxv, 584) discusses the data collected by canvasses made in 40 cities ranging in population from 25,000 to 600,000 and smaller communities. Five thousand or more persons were canvassed in each locality. The rate of attack in various communities varied from 185 per 1000 to 535 per 1000; this was without special relation to geographic location or size. The attack rate was highest in the age group 5 to 9 and declined with increasing age, except for the groups 25 to 34, in

which the incidence was higher than in the group 15 to 24. Almost uniformly the rate was higher for women than men and lower for the negro race than for the white. The latter is surprising in view of the normally high incidence of respiratory infections among negroes. The case fatality varied from 3.1 per cent. to 0.8 per cent., being generally higher on the North Atlantic seaboard and the Pacific Coast. The case fatalities differed for different age groups and was generally higher among negroes than among whites.

The Experimental Production of Pneumonia with the Influenza Bacillus of Pfeiffer.—MAJOR (*Jour. Med. Research*, 1920, xli, 373) states that the results of the experiments undertaken in his study indicate that the invasive powers of B. influenzæ are limited. When the organisms are injected intravenously the effects produced are to be explained by a toxic action rather than any direct bacterial action produced by multiplication and spread through the blood stream. In no cases were the bacilli recovered from the blood cultures in animals which had been injected intravenously with influenza bacilli. Introduction of B. influenzæ into the trachea was successful in producing bronchopneumonia. In these cases, also, the invasive properties of the organisms were apparently limited, as the bronchopneumonic patches were small, few in number and confined to the hilus of the lungs. The location of these areas also suggested a local direct action of the masses of bacteria, with but little extension to other portions of the lungs. In contrast to the results obtained by the intravenous and intratracheal introduction of the bacilli a preliminary irritation of the respiratory tract with chlorin gas permitted an extensive invasion with influenza bacilli injected intravenously or intratracheally. The pathological changes produced in the lungs were striking and intense in degree and resembled the lungs in fatal cases of human influenza. In the majority of these cases influenza bacilli were grown from the lungs in pure culture.

Tellurium as a Health Hazard in Industry.—SHIE and DEEDS, (*Public Health Reports*, No. 16, 35, 939) present evidence on the importance of tellurium as an industrial poison. The element tellurium resembles metals physically, but chemically is related to sulphur and selenium. It is used in the production of colored glass. The cases of poisoning in question were among employees of a silver refinery and were men who were exposed to fumes and dust containing the poison. The main channels of entry are by the respiratory and alimentary tracts, but the skin probably absorbs some. In the body this poison becomes converted into a compound which imparts a garlic-like odor to secretions and excretions. The poison is eliminated through feces, urine, lungs and skin. The symptoms are summed up as follows: "Garlic odor to the breath, sweat, and alvine discharges, dryness of mouth, metallic taste, nausea, anorexia, loss of weight, constipation or diarrhea, suppression of the sweat, and a dry, itching skin. Associated with these symptoms are likely to be a hypoacidity of the gastric juice, with a mild gastro-enteritis and parenchymatous nephritis. Inasmuch as the symptoms of mild tellurism are the same for man and the laboratory animals, we have reason to believe that the more severe effects, as well as the pathological changes, would likewise be similar. As yet

we have met with no severe cases of tellurium poisoning; but we should expect such cases to exhibit violent vomiting, purging, intestinal hemorrhages, loss of reflexes, tremors, extreme depression, and finally paralysis of the central nervous system, with unconsciousness, dyspnea, and at last death in convulsions. Associated with these symptoms there would be destruction of the red blood cells, decreased hemoglobin content, hemorrhages into the various organs, and a severe gastroenteritis and nephritis." The hazard seems to be high, as more than half of the men exposed to the fumes showed evidence of poisoning. The prevention lies in the observance of precautions applicable to other metallic poisoning, such as adequate ventilation, use of respirators, proper washing and drinking facilities. Full coöperation on the part of the employee is necessary. The prognosis is good, and treatment consists of eliminative and supportive measures.

Recent Work on Pellagra.—VOEGTLIN (*Public Health Reports*, No. 25, 35, 1435) reviews the history of pellagra and refers especially to the limited geographical distribution. Attention is called to the fact that clinical observers long ago laid the foundation for the latter-day research that has been so fruitful, as follows: "Thus Casal, Strambio and others speak of the good results obtained with a mixed diet. Roussel, in his admirable *Traité de la Pellagre*, states that the real treatment of pellagra is a milk diet, and supports this statement by the histories of a number of cases which were evidently cured by a liberal diet. Lussana and Frua (1856), on the basis of over 8000 cases treated with a liberal mixed diet, claim that the mortality fell from 24.5 to 4.5 per cent., and that the recovery rate increased from 20 to 75 per cent. as a result of this treatment. The value of the dietary treatment was therefore well established and almost universally accepted even by the adherents of the infectious and "spoiled-corn" theories. This was a most significant fact, which gained in importance when it was brought into relation with the characteristics of the diet consumed by persons prior to their attack of pellagra. The striking features of this diet appeared to be its lack in certain animal foods, such as milk and meat and eggs, the same foods which proved to be so beneficial in the treatment of the disease." Attempts at producing the disease in animals are described as well as studies of metabolism. The evidence of the dietary deficiency that is responsible for the disease is fully described. Vitamine deficiency is less likely than "that the pellagrous syndrome is caused by *a combination of the deficiencies in some of the well-recognized food factors*, a hypothesis which would account, first, for the resemblance between the symptomatology and histopathology of scurvy, beriberi, and pellagra, and, second, for the great individual variation in the symptom complex observed in different patients. The precise nature of the dietary deficiency remains to be discovered.

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